MERCURIAL DIURETICS

INTOLERANCE AS SHOWN BY SKIN SENSITIVITY

BY

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The rarity of adverse effects following the use of mercurial diuretics is remarkable, considering how widely they are now employed. Many regular recipients with heart failure and, less frequently, with renal œdema would at least be confined to their beds but for these preparations. The causes of the few complications reported have been uncertain and idiosyncrasy or allergy has often been given as an explanation. Having seen many cases who receive doses of this drug with impunity for years, the temptation is to dismiss the explanation of simple accumulation. A hitch in a standard regime, however slight, is often interpreted as a contra-indication of the further use of a drug, although the cause of the untoward effect is not known. Such an abandonment in the case of mercurial diuretics frequently leads to a deterioration of the patient's health, and a fuller understanding of such reactions is therefore important.

Wolf (1931) reported a case of sudden death following intravenous salyrgan in a child aged four, with nephrosis; the injection preceding the fatal one caused a chill, fever, a morbiliform rash, and anorexia; but resulted in satisfactory diuresis although previously the output had been disappointing. Keith (1936) stated that injections of organic mercury might be followed by stomatitis, diffuse dermatitis, diarrhœa, hæmaturia, and renal insufficiency, but considered that these reactions were rare. He also noted that if the mercurial diuretics were discontinued for about ten days the drug could often be given again with satisfactory results. Klein and Seymour (1942) discussed several cases with skin reactions. In one, urticaria appeared after eight consecutive injections at unstated intervals, and an evanescent erythema followed the final two injections in this case. A transient erythema was seen in others, one of which after further salyrgan injections developed an " inflammatory reaction of the skin which progressed to a typical exfoliative dermatitis." In their opinion these cutaneous manifestations were warnings of more serious reactions to follow, and contra-indicated further use of the drug. A discussion of cutaneous eruptions produced by mercurial diuretics with many references is to be found under the names of De Graff and Nadler (1942). Types of reactions so produced include urticaria, small reddish spots or purpuric areas, and morbiliform or scarlatinaform erythemata; occasionally the rash was followed by desquamation in one to three weeks. They suggested that positive patch tests indicated an allergic basis and that although an accumulation was seen with the older type of mercurial diuretic, it did not occur with the rapidly excreted theophylline-containing mercurials. They also pointed out that an erythematous skin eruption may follow either the first or any subsequent injection of the diuretic. Relationship to dosage or excretive response was, however, not considered. Other theories have been suggested. According to Lesser (1888) peripheral vasodilatation is caused by the paralysing effect of mercury on the sympathetic nerves. The histological studies of Almkvist (1922) also indicate the cutaneous capillary dilatation is caused by mercury. Their studies of the reactions produced by mercurial diuretics in a woman, aged 27, with rheumatic heart disease were reported by Fox, Gold, and Leon (1942). Several mercurial preparations were found to affect her similarly and their experiments showed that the xanthine content of these substances was not to blame.

Engel (1937) quoted by Barber (1938) stated that novurit suppositories " should not be given at an interval of less than five days. Adherence to this rule renders the patient tolerant

of repetitive suppositories over a period of years without the production of a chronic inflammatory reaction in the rectal mucosa." This statement suggests that frequent application of the mercurial may lead to sensitization. Barber considers that signs of mercurial poisoning are "a sequel to failure of elimination when, as sometimes happens, diuresis does not occur." The effects which manifest themselves include stomatitis, diarrhœa, vomiting, hæmaturia, and purpura. Evans and Perry (1943) mention skin rashes caused by mercurial diuretics but do not associate them as forerunners of more serious things. Other authors have commented on the freedom of this treatment from serious complications (Evans and Paxon, 1941). We report the following new cases of skin erythema following the administration of mercurial diuretics.

Case Reports

Case 1. A trolley bus conductor, aged 48, had essential hypertension with heart failure. Dyspnœa on exertion and nocturnal asthma started in 1942, and œdema of the legs in November 1943; from that time onwards he received from his private doctor 2 c.c. of neptal intravenously, three times a week with a good but diminishing diuretic response. In February 1944 a faint generalized pink rash with irritation was noticed, which steadily increased with each injection. He was then referred to one of us (A.B.). A positive patch test to neptal confirmed the suspicion that the rash was caused by that drug. A control test on a student was negative. The use of neptal was accordingly discontinued and the rash gradually faded. The patient's symptoms of cardiac failure, however, soon returned. By June, nocturnal dyspnœa was severe and so neptal was given again in doses of 2 c.c. twice a week. No recurrence of the rash or irritation took place. From July 1944 until his death in December, he was under our observation. Apart from a weakly positive result in August, patch tests frequently repeated, proved negative, as did similar tests to other organic mercurials including mersalyl, esidrone, and salyrgan. Although severe failure rendered necessary the use of frequent mercurials, neptal 2 c.c. every third or fourth day, and rest in hospital, the original dosage of 6 c.c. in a week was not employed from February 1944 onwards, and the diuretic response was excellent varying from three to four pints. It would appear that this man could tolerate 4 c.c. of neptal weekly as long as his elimination was satisfactory, but that 6 c.c. in a week over a period of 3 months with less efficient diuresis led to accumulation and skin manifestations. After a rest of three months, but without any active densensitization he showed no reactions to further injections and only a faintly positive patch test on one occasion.

Case 2. A woman, aged 39, was first admitted to hospital with nephritis (Type II, Ellis, 1942) in January 1943. Œdema of the nephrotic type was gross. The blood pressure was 180/100. There was no heart failure. The urine was loaded with albumin. The blood area was normal, and the plasma protein 4·6 mg. per 100 c.c. Rest, limitation of fluids, and a high protein diet did not alter the plasma protein and the œdema remained. Neptal, 2 c.c. intramuscularly was therefore started on February 22, 1944 and given every fourth day preceded by 30 grains of ammonium chloride by mouth. The diuretic response was disappointing and seldom exceeded 50 oz. This dosage was continued until May 1943 when the œdema of her legs which had persisted, increased greatly. She was therefore rested once more as an inpatient and the effect of 3 c.c. neptal intramuscularly was observed. At four daily intervals three such injections did not meet with proportionate outflow, and so the dosage was returned to 2 c.c. twice weekly, while she attended as an outpatient. Readmission was again necessary in October 1943. Her œdema was worse and her plasma protein still low (4 mg.). The hæmoglobin was 104 per cent. Within two months she had lost one stone in weight. Before her discharge on December 24, 1943 the dose of neptal was increased to 2·5 c.c. twice weekly with improved but only moderate response. This dosage was continued from outpatients until February 26, 1944 when an injection was followed by a generalized itching with erythema, mainly of the upper limbs and thighs. On March 6, mersalyl 2 c.c. was substituted, but this again produced itching and enhanced the rash. Mercurial dermatitis being suspected, a patch test of neptal (full strength) with saline control was carried out and this was positive when observed after 48 hours. The diffuse rash was now dry, fine, scaling, and less pink. After mercurials had been discontinued for two months, a further patch test was found to be negative. Salyrgan 2 c.c. was tried on May 4, this only produced an output of 2 pints but there was no skin reaction. She returned to neptal 2 c.c. twice weekly but the injection on May 13 was followed four hours later by a return of the itching rash, which spread up to the arms from the wrists. Within the next 48 hours a slight recurrence was also noticed on the neck and thighs. The rash was red to pale pink, punctate, macular, and sometimes confluent. Dry scaling patches up to 0·5 cm. diameter in both anticubital fossæ dated from the previous rash was much more severe. Her output to the last injection produced 60, 56, and 38 oz. on consecutive days, during a daily intake of 30 oz.

Three days after that injection her blood count showed an eosinophilia of 5 per cent which might have indicated an allergic reaction. A patch test that same day was uncertain, as some redness was caused even by the control owing to the irritable state of her skin. Ten days after that injection, the rash was coarser, and more powdery, involving upper limbs, buttocks, thighs, and neck. Itching was still intense. By June 6, the rash had spread down to the legs although improvement was apparent

elsewhere. The most severe areas, the inner side of the forearms, then received 100 r unscreened X-rays with marked benefit, and this was followed one week later by similar dosage to the outer aspect of the arms. By July 4 the rash had nearly gone; patch tests to 25 per cent solutions of neptal, mersalyl, salyrgan, and esidrone with saline control were applied and these were all still negative after three days. Full strength patches of these mercurials applied on July 17 were also negative. Her skin had therefore become negative to patch testing in just over two months from the last injection of neptal, although no desensitizing doses had been employed. From July 18 at weekly intervals other mercurial diuretics were injected including esidrone 1 c.c., mersalyl 2 c.c., and salyrgan 2 c.c., and no skin reaction occurred. Finally neptal was again used with satisfactory effect in 2 c.c. dosage at weekly intervals, from August to September when a patch test was again negative. An improvement occurred in her condition at this time. The œdema diminished rapidly, and no further mercurials have been required.

It would appear that this patient tolerated 2 c.c. neptal twice weekly for ten months without any adverse effect in spite of poor diuresis, but after eight weeks of 5 c.c. instead of 4 c.c. in each week, a rash appeared. After two months without injections, she could tolerate further mercurials for a time, and her patch test was negative. The second skin reaction took six weeks to clear completely, and by this time she was again patch test negative.

Case 3. A woman, aged 63, was first seen in June 1943 suffering from hypertensive heart failure and auricular fibrillation. The blood pressure was 210/130 and there was aortic valve disease. Besides digitalis and reduced fluid intake, her treatment included weekly intramuscular injections of 2 c.c. of neptal. Although the diuretic response was not satisfactory, improvement was maintained until eight months later when she complained of intense generalized itching of the skin with a weeping rash of the thighs and arms. Neptal was discontinued and her skin condition cleared. As the œdema returned, Guy's pill (powered squill, digitalis, calomel, gr. i) was given three times daily. After two weeks the patient noticed a recurrence of the rash on her left thigh and this spread rapidly to form a band about six inches wide almost encircling the limb. Soon the generalized itching returned, it was therefore decided that the Guy's pill, containing mercury to which she was apparently susceptible, must be discontinued in favour of tab. digitalis folia. The skin condition improved immediately, but the œdema increased. Three further doses of Guy's pill caused an exacerbation of the rash, which confirmed the observation that oral administration of the mercury was to be blamed.

Four months later the patient was again seen in consultation. Her ascites and œdema were gross, a patch test to neptal was negative. Mercurial diuretics were not again tried until late in November 1944 when 1 c.c. neptal resulted in a urinary output of 83 oz. Subsequent doses at long intervals were not followed by cutaneous complications.

Case 4. This man, aged 58, was first seen in consultation in April 1944. Ten years previously he had undergone subtotal thyroidectomy and now showed evidence of hypothyroidism. The history and cardiogram also suggested a cardiac infarction one year previously. The blood pressure, 115/105, which rose to 230/170 under observation, breathlessness, œdema of ankles, and pulmonary congestion provided evidence of heart failure. Commencing on April 19, 1944 he received 2 c.c. neptal intramuscularly twice a week for 3 weeks, then once a week until June 14, 1944 after which injections were given every fortnight. His urinary output was not recorded but, satisfactory at the start, it diminished latterly. On August 1 he developed a diffuse rash over his abdomen, thighs, and the outer aspects of the arm. Intense itching accompanied the rash which was worse a few days after the injection. A neptal patch test was positive when removed after three days, an irritating erythema underlying the gauze square. His wife who was acting as control showed a completely negative result. Neptal injections were then recommenced once a month with satisfactory diuresis and no return of the cutaneous complication.

Although the injections were infrequent compared with those received by some other cases, possibly accumulation of mercury occurred because the diuresis after each dose was insufficient to ensure elimination. The individual tendency of such a patient to sensitization, however, must be taken into consideration.

Case 5. A woman, aged 53, was admitted to hospital with mitral stenosis, auricular fibrillation, and chronic heart failure. One week later, as her improvement with rest, adequate digitalization, and reduced fluid intake was not satisfactory mercurial diuretics were started. The first injection, 2 c.c. neptal intramuscularly, produced a diuresis of 104 oz. and a diminishing but satisfactory output continued over the next few days. On the third day after the first injection, neptal was repeated, this time producing 122 oz. in the subsequent 24 hours, with marked clinical improvement. After a further five days a third dose only gave a response of 68 oz. and about 1½ hours after this she vomited and complained of generalized itching No rash was seen although a careful watch was kept. Owing to an oversight the mercurial diuretics were not discontinued, and three days later a fourth injection of 2 c.c. neptal caused a similar irritation without a rash. A patch test applied after a lapse of three days showed a faint erythema with pin head vesicles; a control of saline was negative, as well as a neptal patch applied to a patient not receiving mercurials.

As the third injection met with a fair response only, a longer interval might have been allowed to elapse before the next injection. Itching of the skin too should have been sufficient warning that accumulation of the drug and sensitization of the skin were occurring.

Case 6. A man, aged 21, was admitted with heart failure and auricular fibrillation from mitral stenosis and aortic incompetence with stenosis. As the liver reached the umbilicus and ascites was starting without much peripheral œdema, congestive cirrhosis of the liver was suspected. Neptal intramuscularly in 2 c.c. doses twice a week had met with satisfactory diuresis from three weeks until one day before admission, when the last injection by the private doctor had proved inefficient. After admission and four days after the last mercurial, the same dose was given intravenously after premedication with ammonium chloride, with good diuresis. The injection of October 12, 1944 gave a response of 6 pints; but on the 16th no diuresis resulted. The next day the patient was drowsy, incontinent, with generalized œdema including the face, but with no orthopnœa. A diffuse blotchy pale pink rash had developed on the anterior aspect of the trunk, but no mention of itching was made at that time by the patient, possibly because of his mental torpor. Twitching of muscles, a blood urea of 140 mg. and an increase in albumin with a strongly positive guaiacum reaction in the urine, told of acute nephritis which was attributed to the mercurial treatment. The blood pressure, previously varying from 140/50 to 150/70 rose to 200/100 on October 13, and fell to the previous level after four days. A neptal patch test on the arm was then negative as were scratch tests, but a second patch test applied on the 19th in the scapular region was positive.

Normal rhythm was regained on October 19 and the patient's general condition improved. On that date, however, three days after the unsuccessful injection, the rash was more pronounced, particularly on the abdomen. The face was less puffy, and cerebration was clearer, but the breath was fœtid owing to stomatitis. During the next week the rash gradually faded. The urinary output equalled the intake (30 oz.) and the albuminuria diminished. Subsequently the nephritic element improved rapidly, and from the 25th the urine was reported clear. Œdema was still gross in spite of improving output, and so on October 29 a patch test to neptal having been found negative, 1 c.c. was given intramuscularly. This met with an excellent response. The trunk was now almost clear of rash which, however, still remained in a maculo-papular form on the extremities. On November 3, 36 hours after a further intramuscular injection (2 c.c. neptal) a papulo-erythematous rash recurred over the extremities and trunk with great itching. A patch test again proved positive. Eight days later, another neptal injection was tried with entirely satisfactory results and no untoward effects. The rash was now fading but scaling. Œdema of the lumbar region was still gross. Subsequently the use of neptal was continued intramuscularly at weekly intervals, and patch tests were always negative before each injection. The diuretic response varied between 90 and 130 oz. Ascites required paracentesis although peripheral and pulmonary œdema was controlled satisfactorily considering the severe degree of cardiac failure. Recently a trial of Guy's pill, one thrice daily, was made without effect, and was discontinued after five days. At the end of this trial course 2 c.c. neptal produced a diuresis of 186 oz. and a patch test to neptal was negative.

The mercurial preparation not only showed the presence of sensitization in this case, but also produced stomatitis and probably an acute nephritic reaction. All these ill effects were overcome by reduced dosage and careful administration of the drug. Had neptal been abandoned, it is doubtful whether this patient would have left his bed; as it was, he led a quiet life as an out-patient until a sudden decline at the end of April 1945. All excess fluid was eliminated satisfactorily, except the ascites, caused by hepatic cirrhosis for which occasional tapping was required.

Case 7. A male, aged 47, was admitted under the care of Dr. Horace Evans in December 1941. He was a case of insidious nephritis (Type II, Ellis, 1942). A left nephrectomy had been performed in 1922 for renal tuberculosis. His renal efficiency tests showed slight impairment (blood urea 50 mg. per 100 c.c.) In January 1942 before his discharge he received one injection of neptal 2 c.c. intramuscularly with a response of 102 oz. (intake 48 oz.). He was under observation as an out-patient with a varying œdema of the ankles but received no further mercurial injections until January 1944. Two injections at an interval of one week were then followed by the administration of neptal tablets by mouth, the dose of which was 2 t.i.d. for two days in each week, after a preliminary trial of 1 t.i.d. on the first occasion. This dosage was continued until March 15 when it was noted that the tablets caused " a lot of acid " and retching. The intramuscular preparation was therefore recommenced instead of the tablets. Œdema was now increasing steadily. On April 5 the urinary output was 5 pints and his blood urea 48 mg. per 100 c.c. The diuretic response to neptal continued to be satisfactory, reaching 10 pints on May 13 and 4 pints on June 14. On July 26 an itching of the skin was treated by calamine lotion, but neptal continued in the previous dosage (2 c.c. weekly) until he was referred to one of us (A.B.) on September 6. There was a generalized symmetrical rash and œdema of his legs was slight, so it was recommended that mercurial diuretics should be omitted. On October 5 the rash was fading well, and patch tests which unfortunately had been previously omitted, were now negative both on the arms and at the site of the injection (buttock).

In spite of some degree of renal insufficiency, mercurials had been well tolerated from January until July 1944, although it is likely that renal impairment led to an accumulation of mercury over several months. The persistent œdema required the continuation of this regime, and, in the light of our experience since this investigation started, this patient would probably have continued to tolerate mercurial treatment had the interval between the doses been increased.

Case 8. A male, aged 54, was admitted with hypertensive heart failure on January 19, 1945 (B.P. 200/140). His urine was clear, and his blood urea was 58 mg. Œdema was extensive in the lumbar region and lower limbs. Cardiograms supported the diagnosis of hypertension without coronary obstruction.

His first neptal, 2 c.c. intramuscularly on January 25 was followed by a urinary output of 90 oz. Two days later a similar dose produced no diuresis, but output exceeded the fluid intake of 30 oz. by 12, 32, and 30 oz. on that and the subsequent two days. Two days after the second injection, he complained of generalized itching. His blood urea then was 62 mg. and his B.P. 160/90. As his œdema was increasing and a left pleural effusion had developed, neptal was given on January 31. Within three hours of this a morbiliform rash was noticed over his trunk and limbs. The urinary output that day only exceeded intake by a few ounces, and next day rectal incontinence disturbed the fluid measurement. No satisfactory diuresis resulted. A patch test applied 44 hours after the onset of the rash, was negative in 24 hours, but positive in 48 hours. The patient became worse and died on February 7. At autopsy there was no evidence of nephritis and signs of hypertensive heart failure were present.

Case 9. A retired clergyman, aged 83, was admitted to another hospital in August 1944 with coronary thrombosis. Three weeks later œdema slowly developed. From September 2, 1944, mersalyl 1 c.c. was given intramuscularly at weekly intervals. The diuretic response varied from 80 to 100 oz. in the 24 hours and the fluid intake was about 2 pints. Although œdema was not gross, it persisted in spite of prolonged rest and other adjuvants such as digitalis. From October 28 mersalyl 1 c.c. was injected twice weekly, and the urinary output was recorded as between 60 and 84 oz. but for one poor response of 30. During this period the fluid intake was 35–40 oz. daily. The next two injections within one week were of mersalyl in 2 c.c. dosage, and these resulted in 58 and 62 oz. in the following 24-hour periods. From November 4 the mercurial employed was neptal 2 c.c. intramuscularly twice in a week, with diuretic measurements varying between 55 and 107 oz., averaging 78, for the next nine weeks.

In January 1945 the patient's condition was much the same, but he had left bundle branch block. Neptal was continued twice weekly, preceded by three doses of 15 grains of ammonium chloride. The urinary response was recorded as varying between 40 and 100 oz. in the 24 hours, the average output being 59 oz. During that period of five weeks the fluid intake was variable, sometimes reaching 50 oz., and on one occasion 4 pints, although generally being less than 40 oz. From February 12 the injections were given somewhat irregularly, on February 19 and 21, on March 1, 9, 13, 16, 20, and 23. The diuretic response during this period varied between 55 and 66, averaging 58 oz., the daily fluid intake was fairly constant at 35 oz. and without neptal the output was 30 oz. in 24 hours.

On the day after the last injection, an erythema was noticed on the patient's feet, legs, and back. This rash was accompanied by itching and slight diarrhœa. A patch test applied three days later was found to be positive after 48 hours. His urine, usually clear, contained a cloud of albumin with granular and hyaline casts and gave a positive guaiacum reaction on March 27, but was again reported albumin free a few days later. An X-ray of his chest on March 29 showed enlargement of the left ventricle but no hilar congestion. The blood urea on April 6 was 60 mg. per 100 c.c., his blood count was later reported as 3,980,000 red cells and Hb. 80 per cent, and his plasma protein 5·4 (albumin/globulin ratio 1·7).

After a negative patch test, one further dose of 2 c.c. of neptal was given, eleven days after the last injection. There was no diuretic response (output 30 oz.), neither was there any recurrence of rash, albuminuria, or diarrhœa.

It was obvious from these investigations that the œdema was not now caused by heart failure, although initially it may have been so. The falling diuretic response to continued frequent injections of mercurial seemed to assist accumulation of the metal, and skin sensitization.

Discussion

Many patients with sustained high dosage show no signs of intolerance to mercurial diuretics; in fact, the incidence of such manifestations is rare. Numerous patients with heart failure receive full doses of neptal once or twice a week for periods of two or three years without the slightest ill effect. On the other hand, a few cases that have been reported show immediate acute sensitization to mercury, as mentioned by De Graffe and Nadler (1942). Sundaram reported sudden death in a boy of ten years with rheumatic heart disease after the first injection (0·5 c.c. salyrgan in 10 c.c. saline intravenously), but it is not yet proved that such accidents are allergic in nature.

Sensitization, idiosyncrasy, or allergy may be of different degrees. In one of our cases (Case 6) a severe skin reaction was accompanied by manifestations of an acute nephritic nature and by stomatitis. The other eight who received mercurial diuretics only gave the skin signs. It is therefore suggested that rashes and itching are evidence of a moderate degree of sensitization and might be followed by grosser complications if administration of the drug is unscientifically continued.

A positive patch test is a sign of idiosyncrasy or allergy and is accepted as such by practically all the leading authorities. According to Sulzberger (1933), " whenever a reaction of eczematous character is produced at the site of the application of the patch, provided a

substance has been used that is not a primary irritant " (presumably, in the strength employed) " one may conclude that eczematous hypersensitiveness of the skin to this substance has been demonstrated." Patients who have received mercurials for many months or years without any symptoms related to the skin have in our experience shown negative patch tests without exception. There is as yet no evidence that patients exhibiting cutaneous manifestations of intolerance are patch test negative before starting treatment. A routine patch test in a series of cases before injections are started, would decide this point; but, although primary idiosyncrasy has been reported, it is expected that such initial investigations would support the theory of acquired sensitization in the majority of cases. There would appear to be a threshold of concentration of mercury in the blood below which no signs of allergy are given, but above it they are positive. One of the earliest works on sensitization to drugs was by Jadassohn of Breslau, *A Contribution to the Study of Dermatoses Produced by Drugs* (Translation, 1900). It pays much attention to the cutaneous complications of mercurial treatment. In the main, little changes have occurred in the principles underlying the phenomenon of sensitization set out in that work, reference to which proves of great interest in this present problem; for instance, " the remarkable fact already confirmed from observation on the action of mercury and other remedies, that at first a certain cumulative action was necessary to bring out, so to speak, the idiosyncrasy . . ." Similarly, Bloch, quoted by Goldsmith (1936) wrote " idiosyncrasy is only a relative term depending not only upon the nature of the substance but also on its concentration." That accumulation of the drug in the body precedes skin sensitization, as suggested by Barber (1938), seems likely from the consideration of our own cases which tend to show a common factor, namely deficient elimination compared with the amount of drug administered. This may be caused by high or too frequent dosage, as in Cases 1, 2, 5, and 9, and assisted by renal impairment from long standing nephritic damage as in Cases 2 and 7 or from congestive changes as in Case 8, and possibly in Cases 3 and 4. Prolonged administration naturally must tend to produce accumulation of the drug; although with good diuretic response and suitable dosage it is our experience that this factor alone seldom leads to sensitization from the mercurial diuretics. The degree of susceptibility, however, must vary with each patient; for instance, in Case 6 although the previous injection had produced 120 oz. of urine and the patient was still grossly œdematous, the next injection caused an allergic reaction affecting the skin, kidneys, and mouth. Also, we have as yet no conclusive evidence that a good diuretic response assists the elimination of mercury. Quantitative estimations of this substance in the blood and urine are desirable.

From our observations it would appear that sensitivity, as shown by patch testing, may be lost after a brief period of rest from the drug and without desensitizing doses. This fact was noted by Jadassohn who remarked " cases are reported that seem to prove that idiosyncrasies may disappear in the same way as they have been acquired." Goldsmith (1936) was also of this opinion and he wrote " phases occur in specific super-sensitiveness in which the exhibition of allergen no longer causes any material effect." That transient conditions, such as threshold concentration and renal impairment, play a part is also suggested by this author's comment that " allergic disorders depend on other factors, often temporary ones, besides specific sensitization." So far, we have not met the patient who required densensitizing doses of mercury such as those employed by Tate and Klorfajn (1944) with sulphonamides.

Sensitization of one tissue to a substance contained in the body is not necessarily accompanied by a similar condition in other tissues. In our investigation we have employed the patch method of testing for cutaneous sensitivity. Our technique has been as follows. A small square of gauze dressing, about one inch wide and four or five layers thick, is soaked in the test solution (full strength neptal supplied for intramuscular injection) excess of which is expressed. This patch is placed on the skin, and covered by a larger square of dry lint, the two then being held in position by a still larger piece of elastoplast. Thus if the adhesive substance causes any irritation, the resulting cutaneous change will not be contiguous with the central square of positive reaction but separated from it by a normal area protected by lint.

It will be seen from our case reports that a positive patch test was not always obtained at the onset of itching or a rash. Case 6 exhibited a negative reaction on the arm to a patch

applied 24 hours after the onset of the abdominal rash although a positive was produced in the scapular region 48 hours later. Perhaps this observation may have been the result of a technical error. In all the other cases tested, a positive patch test followed the cutaneous symptom although such tests often became negative before the skin was clear.

The patch test would seem to have a useful application, in the treatment of patients with heart failure by mercurial diuretics. In no patient under our observation has an injection of a mercurial diuretic caused a rash when a patch test immediately preceding it proved negative. Accordingly this test should be useful when accumulation of the drug is suspected or when continuation of treatment is desirable after cutaneous sensitization.

In conclusion, it is suggested that cutaneous sensitization to mercury need not contraindicate the subsequent employment of these diuretics in adjusted dosage after a short interval.

Summary

Nine cases of skin reactions to mercurial diuretics are presented.

Many patients with sustained high dosage show no signs of intolerance to mercurial diuretics.

Sensitization, idiosyncrasy, or allergy may be of different degrees. Skin rashes and itching without other complications would seem to indicate moderate sensitivity.

There would appear to be a threshold concentration of mercury in the blood, above which signs of allergy develop, and this may vary with the individual patient.

Accumulation of the drug is assisted by excessive dosage, poor diuresis, and renal impairment.

The patch test is useful in determining the presence of sensitivity of the skin, especially when accumulation of the drug is suspected or when continuation of treatment is desirable after cutaneous sensitization.

The occurrence of cutaneous complications does not preclude further use of mercurial diuretics in adjusted dosage once the phase of sensitization is past.

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THE EFFECTS OF EMETINE ON THE HEART

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The toxic action of emetine on the myocardium in experimental animals is well recognized, but there are conflicting reports on the frequency with which a toxic action occurs in man during the treatment of amœbic dysentery. Manson-Bahr (1939) states that emetine may produce cardiac irregularity and a fall of blood pressure. On the other hand, Brown (1935) at the Mayo Clinic states that myocardial damage is rare, and Heilig and Visveswar (1943) who studied the electrocardiographic changes following the intravenous injection of emetine in 31 cases found no signs of cardiac irregularity, extrasystoles, or heart block. They describe frequent lowering of the T waves in one or more leads, with occasional inversion of T III and T IV.

In the present investigation, changes in the electrocardiogram, blood pressure, and heart rate were studied in patients under treatment for amœbiasis. The patients were otherwise healthy soldiers between the ages of 20 and 40, and in none was there any evidence of wasting or marked toxæmia. In most cases, the standard Middle East Forces treatment for amœbiasis was followed —emetine, 1 grain, intramuscularly, with 2·5 per cent quinoxyl retention enemata, daily for 10–12 days, followed by carbasone, 0·25 g., twice daily for 8 days, and then emetine bismuth iodide, 3 grains each night, for 10 nights. The patients were confined to bed while receiving emetine and emetine bismuth iodide, and serial blood pressure readings were taken during the course. Cardiograms were taken before and immediately after the emetine injection in 32 cases, and before and after emetine bismuth iodide in 8 cases (4 of these had previously received a course of emetine injections and the cardiograms had returned to normal before the emetine bismuth iodide was commenced). It was considered that the influence of quinoxyl could be ignored, as similar changes in the cardiogram occurred when emetine was given alone or combined with the quinoxyl enemata. Owing to shortage of paper, the rate of return to normal of the cardiogram was studied in 8 cases only.

Findings after Emetine

The cardiographic changes in 32 cases following the injection of emetine (total course 8–12 grains) are summarized below.

P wave	No change	21 cases
	Increased amplitude	3 ,,
	Decreased ,,	8 ,,
P–R interval	No change	20 ,,
	Increased amplitude	12 ,,
QRS complex	No change	24 ,,
	Decreased amplitude	7 ,,
	Increased ,,	1 case
T wave	No change	6 cases
	Diminished in one or more leads	25 ,,
	Increased ,, ,, ,,	1 case

Blood pressure. Serial estimations of blood pressure were made in 21 cases. In 13 there was no significant change. Six showed a transient fall of from 15 to 20 mm. in the middle of the course, but had regained their initial blood pressure at the end. In only two cases was there a persistent fall in blood pressure during treatment.

Pulse rate. This showed no significant change in any of the patients under observation.

Findings After Emetine Bismuth Iodide

The cardiographic changes in 8 cases following administration of emetine bismuth iodide by mouth (total course 30–36 grains) are summarized below.

P wave	No change	7 cases
	Increased amplitude	1 case
	Decreased ,,	—
P–R interval	No change	1 ,,
	Increased amplitude	7 cases
QRS complex	No change	5 ,,
	Decreased amplitude	3 ,,
	Increased ,,	—
T wave	No change	—
	Decreased amplitude	7 ,,
	Increased ,,	1 case

There was no significant change in either blood pressure or pulse rate in any case during treatment with emetine bismuth iodide.

Discussion

The cardiographic changes produced by emetine and emetine bismuth iodide are similar. Owing to incomplete disintegration of some brands of the latter supplied, it has been our custom to divide the tablets to ensure that they are dissolved in the alimentary tract, and the occurrence of nausea or vomiting 4–6 hours after administration, suggests that absorption of the emetine has taken place.

The most striking effect on the cardiogram has been the diminution or inversion of the T waves during treatment. This may occur in one or more leads, and is illustrated in Fig. 1 and 2. An increase in the P–R interval of from 0·02 to 0·04 sec. was observed in 19 cases in all, but in no case did the P–R interval extend beyond the upper limit of normal. Changes in the P waves were small and infrequent.

The rate of return to normal of the cardiogram was followed in 8 cases. Changes in the T waves and P–R interval had disappeared in 8–12 days after the completion of treatment in all cases and there was no evidence of residual myocardial damage.

In this series of cases, and in over 250 cases of amœbiasis treated in this hospital, the authors have seen no clinical evidence of myocardial insufficiency during emetine treatment. In this connection it must be stressed that the type of amœbic dysentery encountered in New Zealand troops in the Middle East and Central Mediterranean Forces has been mild. None of our cases has shown evidence of malnutrition or toxæmia, and in all cases the initial

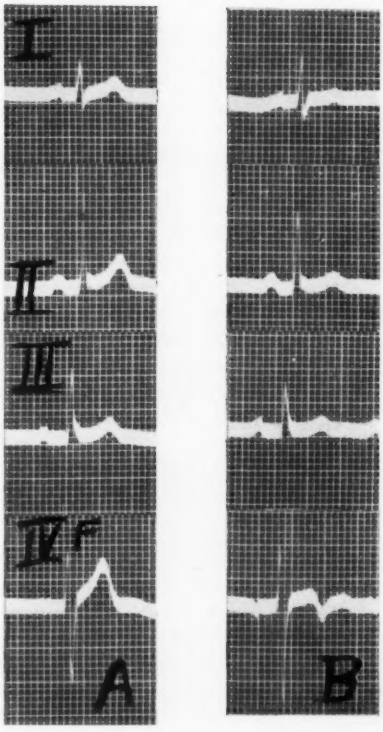

Fig. 1.—Electrocardiograms before and after treatment. Case 16. (A) October 14, 1944, before treatment. (B) October 26, 1944, after emetine, 1 grain for 10 days, showing flattening of T I, T II, and T III with inversion of T IV.

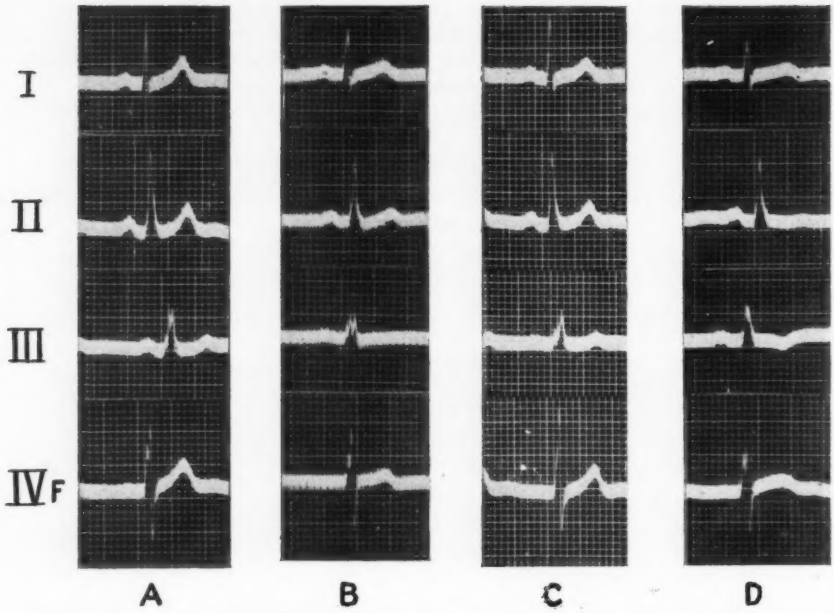

FIG. 2.—Electrocardiograms before and after treatment. Case 16. (A) April 2, 1945, before treatment. (B) April 15, 1945, after emetine, 1 grain for 10 days, showing flattening of T waves in all leads (C) April 24, 1945, showing T waves returning to normal. (D) May 7, 1945, after emetine bismuth iodide, grains 3 for 10 days, showing flattening of T I, T II, and T IV with inversion of T III, and decreased amplitude of QRS in all leads.

cardiogram was normal. Our experience is in agreement with that of Brigadier Bedford, Consulting Physician, Middle East Forces, who, in a personal communication, states that he knows of only one certain case and one doubtful case of toxic action of emetine on the heart occurring in that Command up to the end of 1944.

SUMMARY

Changes in the electrocardiogram, blood pressure, and pulse rate produced by emetine and emetine bismuth iodide have been studied in soldiers under treatment for amœbiasis. All were otherwise healthy and the initial cardiograms were normal. Diminution or inversion of the T waves occurred in one or more leads in 25 out of 32 cases receiving emetine and in 12 cases there was an increase in the P–R interval of from 0·02 to 0·04 sec. Similar changes occurred during treatment with emetine bismuth iodide, 7 out of 8 cases showing diminution in T waves and prolongation of the P–R interval. The cardiogram returned to normal 8–12 days after the completion of treatment. The effect on the blood pressure and pulse rate of both drugs was insignificant, and in no case was there any clinical evidence of myocardial insufficiency.

The authors wish to thank the Commanding Officer of a New Zealand General Hospital and the D.M.S., 2 N.Z.E.F., for permission to publish this article.

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THE CAROTID SHUDDER

BY

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From the Cardiac Department of the London Hospital

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The diagnosis of aortic stenosis in the presence of aortic incompetence needs to be strengthened. A rough systolic murmur in the aortic area is not always accompanied by a thrill. Again, a thrill in the neck cannot be accepted as evidence of aortic stenosis without other supporting signs, especially if the thrill is short and the subject young when a systolic murmur is not expected in the aortic area. In nine patients in whom subsequent clinical, cardiographic, and cardioscopic examination, established the presence of aortic stenosis and incompetence, we observed a characteristic sign, which by itself permitted a diagnosis of the combined aortic lesion from inspection of the neck. At the height of the carotid pulse, large on account of aortic incompetence, we noticed a quiver or vibration which lasted for a moment only. This effect we have named the *carotid shudder* for it best describes the visual clinical sign.

We are not aware that it has been described before, but recently we have read in Paul White's book on *Heart Disease* (1931) a statement that one of his assistants had drawn his attention to a curious vibration in the neck of a young patient with aortic stenosis; there was no mention of associated aortic incompetence, and although it was implied that it was unique and not distinctive for any group of patients, it is probable that the phenomenon was the same as the one discussed here.

The sign was recorded by placing a tambour over the carotid pulsation and connecting it with a Mackenzie's polygraph. Records obtained in this way were examined alongside those obtained in healthy subjects and in patients with lone aortic incompetence or with hypertension producing a kinked carotid. The tracing in carotid shudder, of which that shown in Fig. 1 is representative, was taller than in health, but no taller than the one obtained in

FIG. 1.—Carotid arteriogram in a patient with aortic incompetence and stenosis in whom carotid shudder was observed.

lone aortic incompetence or over a kinked carotid, although it was usually broader and showed characteristic serrations from the vibration or shudder effect. Such vibration usually occurred at the height of the upstroke. None of the control cases showed all three features of the carotid shudder curve, namely tall, broad, and serrated. The tracings, however, failed to portray adequately the characteristic vibration which was so distinctive on clinical inspection of the carotid pulse.

Only a proportion of patients with conjoined aortic stenosis and aortic incompetence exhibit carotid shudder, but the fact that we were able to collect nine such cases during eighteen months emphasizes its common incidence. The clinical sign was sought in patients where aortic incompetence or aortic stenosis existed separately, but it was not found once.

Clinical examination. On further examination of the nine patients the pulse was often collapsing in character with a raised pulse pressure commensurate with the degree of aortic incompetence accompanying the stenosis. Pulsation was often obvious in the suprasternal notch, but never as prominent as in the carotid arteries. There was always a long systolic

thrill in the neck which was felt best above the right clavicle; in six cases the thrill was elicited in the aortic area as well. The apex beat was displaced outwards, and loud systolic and early diastolic murmurs could be heard between the aortic and mitral areas. The ætiology was rheumatic in eight patients and luetic in one.

Electrocardiogram. This was abnormal as a rule, and the changes included inversion of the T wave, depression of the R–T segment, and left electrical axis deviation. The signs of left ventricular preponderance were often present and consisted of left axis deviation, inversion of the T wave in lead I, and greater inversion of the T wave in lead CR_7 than in IVR.

Cardioscopy. The findings included enlargement of the left ventricle in proportion to the degree of incompetence present, outward curving of the ascending aorta, and extension of the left limb of the arc, which formed the aortic knuckle, towards the left clavicle; increased aortic pulsation produced an upward projection of this limb during systole, and displaced the main arc to the right. When viewed in the left oblique position the aortic elongation did not always raise the aortic arch as in hypertension, but it sometimes displaced the limbs of the arch apart and widened the base of the aortic triangle above (Fig. 2). In other cases

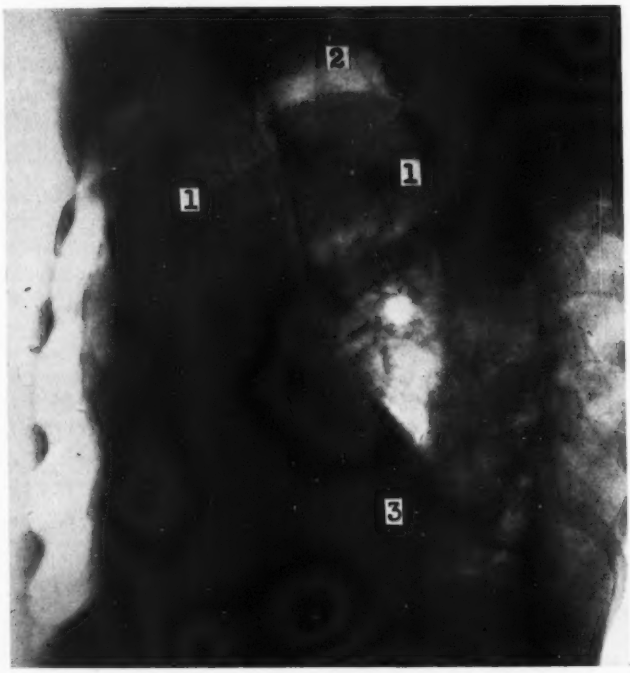

FIG. 2.—Left oblique (II) view in a male, aged 58, with aortic incompetence and stenosis, who showed carotid shudder. Elongation without elevation of the aortic arch (1) has widened the base of the aortic triangle (2). Enlargement of the left ventricle (3) is shown.

the aortic arch was neither elongated nor raised. Such effects show that the mechanism of carotid shudder is not related to any change in the alignment of the artery, but probably depends on an increase in the volume of blood discharged into the vessel with each systole and the impedient effect of the stenosed aortic valve on the returning flow to the left ventricle.

CONCLUSION

When the increased carotid pulse exhibits vibration at the height of the systolic excursion, it signifies that aortic incompetence and aortic stenosis exist side by side. We have named this sign the *carotid shudder*, and although it is not found in all cases of aortic incompetence and stenosis, its presence is a sure indication of the dual lesion.

A QUANTITATIVE ELECTROCARDIOGRAPHIC METHOD

BY

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The sum of the numerous electromotive forces generated during the spread of the ventricular impulse can be regarded as a vector quantity and represented by a straight line of certain length and direction. The angle made with the horizontal by the projection of this vector on to the frontal plane is known as the electrical axis of the heart and can be calculated, by the method of Einthoven *et al.* (1913), from the magnitude of the initial ventricular deflections in two of the limb leads of the standard electrocardiogram.

It is possible to apply this method to an electrocardiogram derived from three points in the sagittal plane of the body, thus identifying in a similar way the sagittal projection of the same vector. From these two projections on to planes at right angles to each other, both the direction and magnitude of the vector itself can readily be calculated.

The present investigation is concerned only with the magnitude evaluated in this way, and was undertaken to explore the possibility of obtaining quantitative information on the state of the ventricular muscle. The values obtained are empirical, as only a small and unknown proportion of the total electromotive force generated by the heart is induced at the periphery and becomes available for measurement. It is not, however, unreasonable to assume that, if obtained under standard conditions, these values will bear a fixed relationship in the same patient to the resultant potential difference generated during ventricular systole.

The Sagittal Electrocardiogram

The derivations of this cardiogram must be so chosen that the projection obtained from it of the vector on to the sagittal plane is concordant with the frontal projection given by the limb tracings. The triangles formed by vertebra prominens, xiphisternum, and sacrum, and by the xiphisternum, twelfth thoracic vertebra, and forehead, were tried and found unsatisfactory in this respect, probably because the xiphisternal point is too close to the heart. A sagittal tracing derived from the triangle formed by the manubrium sterni, fourth thoracic spine, and left leg, with the terminals R.A., L.A., and L.L. connected in this order was found to be suitable and was generally adopted. In this triangle the horizontal lead lies in the same plane as lead I of the standard tracing, and it is also convenient in operation, as the five electrodes for the two cardiograms can be applied at the same time and the change-over effected by a double-pole double-throw switch. As the vector is usually directed downwards and backwards, this arrangement of the terminals gives positive deflections in each of the leads, which will be referred to as A, B, and C respectively. Standard electrodes and Cambridge jelly were used for all the skin contacts.

Calculation. The symbols I, II, III, and A, B, and C, will be used to denote the positive height, in millimetres, of the initial ventricular deflections in the respective leads, or the algebraic sum where the deflection is diphasic.

Fig. 1 shows an imaginary rectangular prism, with faces lying in the frontal, sagittal, and horizontal planes, constructed about the diagonal AG, which represents, in direction and length, the apparent electrical vector of the heart. AF and AC show the sagittal and frontal projections of this vector. Now the length AG is equal to the square root of the sum of the squares on the three dimensions of the prism. The horizontal dimensions AE, AD, have

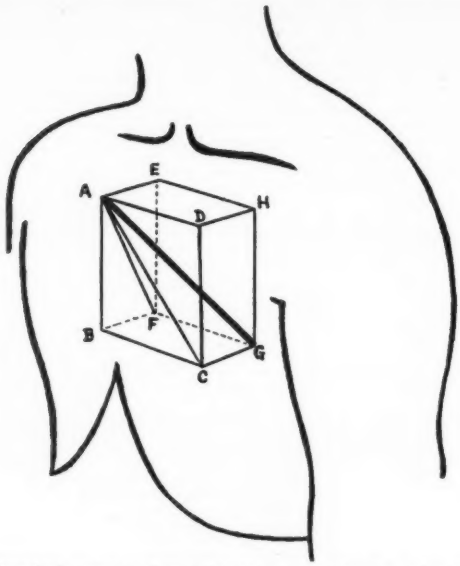

FIG. 1.—The electrical vector and its projections on to the frontal and sagittal planes.

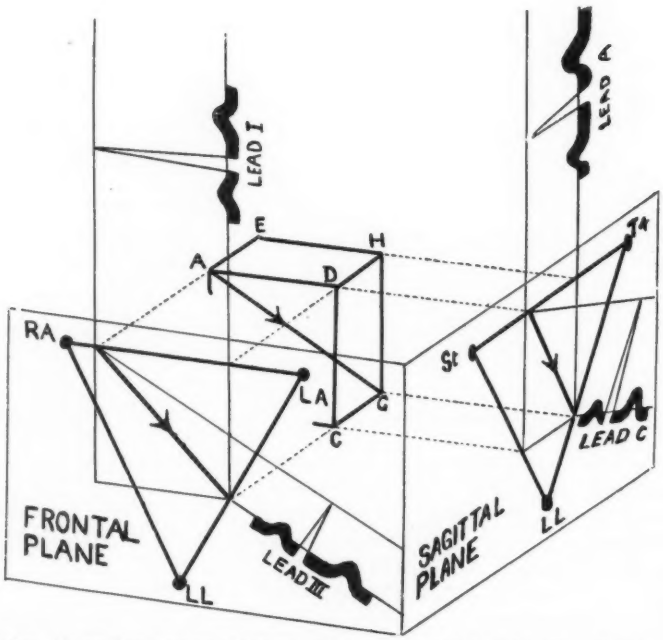

FIG. 2.—Illustrating the construction on which the calculation of V is based. The triangles are equilateral and the lettering A–G corresponds to that in Fig. 1.

the numerical values A and I respectively, and the vertical AB can be calculated from either cardiogram (see Fig. 2) as $\frac{I+2III}{\sqrt{3}}$ or $\frac{A+2C}{\sqrt{3}}$. Hence the length of the vector (V) is:—

$$\sqrt{I^2+A^2+\frac{(I+2III)^2}{3}} \quad or \quad \sqrt{I^2+A^2+\frac{(A+2C)^2}{3}}.$$

These alternative formulæ can be used to check the accuracy of the recordings in a given case. Exact agreement was not expected for several reasons, both theoretical, as the method attempts to simplify very complex phenomena, and practical, such as inaccuracy of standardization, artefacts of various kinds, and respiratory variations in amplitude.

In the 188 pairs of recordings considered here, substitution into the second of these two formulæ gave a higher value for V than was obtained from the first in 56 per cent, equality to the nearest mm. in 30 per cent, and in 14 per cent the first formula gave the higher result. If the difference exceeded one-fifth of the higher figure, the maximum that could be attributed to the summation of instrumental errors, the result was discarded. This occurred in 16 (8·5 per cent) of the cases. Otherwise a mean value for V was taken if any difference existed.

A second check can be made by recording all six leads of the cardiograms instead of only three (I, III, and A or I, A, and C) required for the calculation; inaccuracies of standardization can then be detected by substitution into the formulæ I+III=II and A+C=B.

The usual standard fibre sensitivity of one centimetre deflection to the millivolt was used, but for convenience the values V are expressed in millimetres.

Findings in Normal Subjects

Sagittal and limb tracings were recorded in a series of 50 healthy men and women between 18 and 70 years of age, and the value of V calculated in each. Lying between extremes of 6 and 26 mm., these showed a peak incidence at 11–15 mm., thereafter falling off towards the higher values (see Fig. 3). A figure below 10 mm. was found in only two of these normal subjects; in one of them it was 9 mm., and in the second (6 mm.) the tracings showed an unusual mode of spread of the contractile stimulus through the ventricles. It was not found possible to establish any relationship between an individual's V value and any other physical characteristic such as age, height, weight, height/weight ratio, body surface area, or the size of the heart as estimated by the frontal X-ray area.

Tracings, which were discarded as unreliable by the standards indicated above, were obtained from a further 6 normal subjects. Most of these showed evidence of faulty recording, but their V values, approximately estimated, were found to fall in the same groups of maximal incidence as the rest, and their inclusion would not alter the balance of the chart.

The value of V was not found to change in the same normal subject at different times or at varying pulse rates.

Findings in Abnormal Subjects

The double electrocardiograms were recorded in a series of 101 consecutive patients who were known to have some cardiac disorder and the value of V calculated in each. These cases were as follows :

Rheumatic valvular disease	32
Coronary arteriosclerosis	21
Cor pulmonale	11
Cardiovascular hypertrophy	11
Senile myocardial degeneration	4
Thyrotoxic heart disease	4
Failure associated with anæmia	4
Acute (non-rheumatic) myocarditis	3
Pulmonary embolism (without valvular disease)	2
Syphilitic coronary stenosis	1
Beri-beri	1
Unclassified	7

Ninety-one of these patients were further classified into four grades according to the severity of their symptoms.

0. Symptom-free patients, in whom heart disease was discovered during routine examination.

I. Mild symptoms; e.g. reduced exercise tolerance, or first hæmoptysis in mitral disease.

II. Moderate symptoms; e.g. early congestive failure, or repeated anginal attacks.

III. Severe symptoms; e.g. bedridden patients with advanced failure.

These results, with an analysis of their statistical significance, are given in the table and frequency distribution charts below, where it will be seen that the abnormal cases as a whole show much lower values than are found in health. Taking 10 mm. as a critical point, 45 per cent of the patients give figures below this level, as against 6 per cent of the normal subjects. It is also apparent that the tendency to provide lower V values increases with the severity of the symptoms, and that those patients who are symptomless or only mildly incapacitated show no significant variation from the normal mean. Cases of rheumatic valvular disease and coronary ischæmia have been tabulated separately to show how this tendency is increased in these groups.

TABLE I

ANALYSIS OF FINDINGS IN 151 SUBJECTS

	V value in mm.						Number of cases	Mean V value	S.D. of mean	Difference from normal mean ±S.E. of difference	Degree of significance
	0–5	6–10	11–15	16–20	21–25	26–30					
Normal subjects	0	3	22	16	8	1	50	16·2	4·5		
Abnormal—											
All cases	13	32	35	15	4	2	101	11·7	5·2	4·5±0·83	5
Grades of severity (see text) * I	1	3	8	5	2	0	19	14·4	5·0	1·8±1·31	—
Grades of severity (see text) * II	6	13	19	7	1	1	47	11·6	5·4	4·6±1·02	4
Grades of severity (see text) * III	5	11	4	1	0	0	21	8·2	4·0	8·0±1·08	8
Rheumatic V.D.H.—											
All cases with symptoms	2	8	13	3	2	0	28	12·1	4·9	4·1±1·12	3
Grades of severity 0	0	0	1	2	0	1	4	19·5	4·5	−3·3±2·32	—
Grades of severity I	0	1	4	2	2	0	9	15·8	3·9	0·4±1·41	—
Grades of severity II	0	5	7	1	0	0	13	11·5	2·9	4·7±1·01	4
Grades of severity III	2	2	2	0	0	0	6	8·0	3·9	8·2±1·71	5
Coronary disease—											
All cases	5	7	5	3	1	0	21	10·6	4·8	5·6±1·23	4
Grades of severity I	0	1	1	1	0	0	3	13·0	4·2	3·2±2·45	—
Grades of severity II	2	2	4	2	1	0	11	12·6	4·8	3·6±1·58	2
Grades of severity III	3	4	0	0	0	0	7	5·9	2·4	10·3±1·10	9
Cor pulmonale	2	6	3	0	0	0	11	8·5	3·4	7·8±1·19	7
Failure with hypertension	1	2	10	5	0	1	19	14·1	6·4	2·1±0·86	2
Do. (uncomplicated)	1	1	4	4	0	1	11	14·5	6·9	1·7±2·17	—
Do. (other lesions present)	0	1	6	1	0	0	8	13·0	2·5	3·2±1·19	2

* 91 cases were graded: 4 in grade 0 are not included here.

This measure of agreement between the depression of V and the severity of the symptoms was not found in hypertensive patients except where other complications such as coronary stenosis, cor pulmonale, or valvular disease were present. This may be because of the greatly increased ventricular bulk in such cases, or because of the relative inadequacy of even a powerfully acting heart against the increased peripheral resistance. It is important too to note that 8 of the 19 tracings from hypertensive patients showed the broad initial ventricular deflections of the bundle branch block type. This kind of tracing presents a special source of inaccuracy, because the electromotive force is really proportional to the

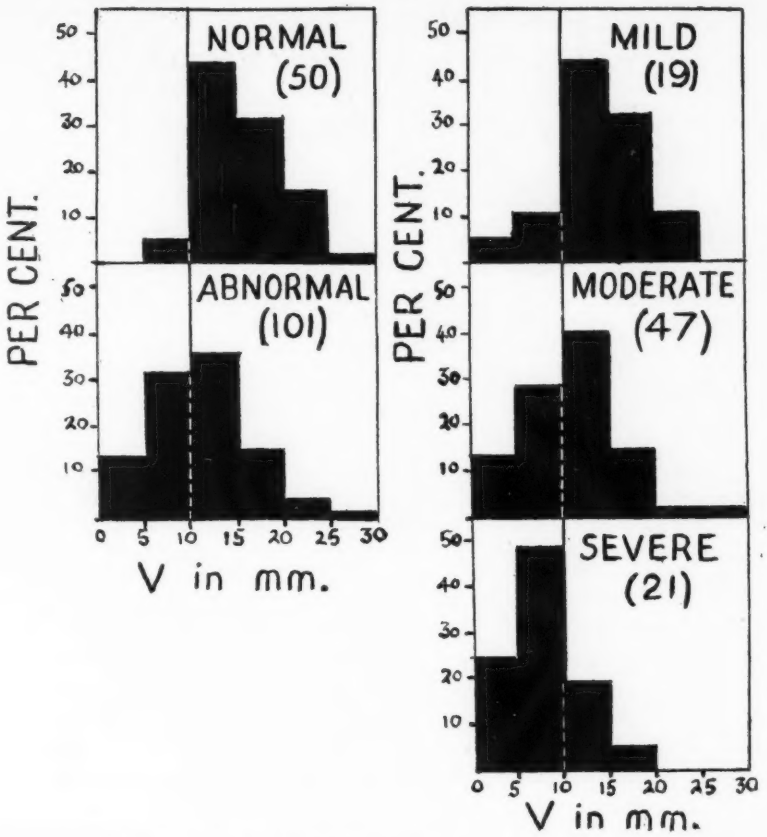

FIG. 3.—Frequency distribution charts to show the contrast between (*a*) normal and abnormal subjects, and (*b*) abnormal subjects graded by severity of symptoms. Bracketed figures show the number in each group.

area contained by the initial deflection, and the use of the linear height measurement is a convenient approximation only reliable with waves of normal duration.

Repeated evaluations of V were made at later dates in 17 of the patients in whom there was evidence that the cardiac capacity had improved or deteriorated in the interim. Of 15 patients with clinical improvement 12 showed a higher value on the later occasion, with increases up to 60 per cent of the original figure in two cases. A difference of less than 10 per cent was disregarded. These 12 cases were of diverse pathology, and three examples will be given.

1. Male, aged 60. 25/1/45. Chronic bronchitis, early cor pulmonale, B.P. 128/80. V=10 mm.

15/2/45. Much improved by rest, B.P. 155/80. V=15 mm. (+ 50 per cent).

2. Male, aged 64. 18/1/45. Pernicious anæmia (hæmoglobin 49 per cent), with congestive failure. V=5 mm.

30/5/45. Hæmoglobin 90 per cent, no evidence of failure. V=8 mm. (+60 per cent).

3. Male, aged 8. 23/5/45. Pharyngitis and cervical adenitis with toxic myocarditis, pyrexia. Cardiogram showed P–R interval of 0·24 sec., occasional sinus arrest. V=13 mm.

31/5/45. Temperature settling. P–R, 0·16 sec. V=17 mm.

7/6/45. Discharged from hospital. Normal rhythm, P–R, 0·12 sec. V=19 mm. (+45 per cent).

The last case is of interest because of the parallel recovery of the A-V block, a guide not always available in acute myocarditis.

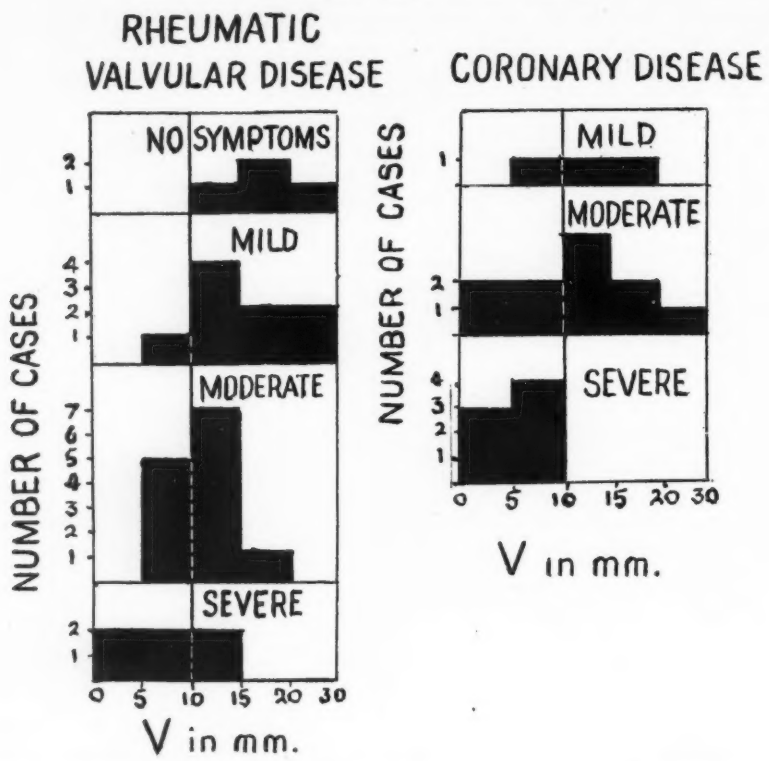

FIG. 4.—Frequency distribution in cases of rheumatic and coronary disease, graded by severity of symptoms.

Of the three cases in which the V value remained unaltered during apparent clinical improvement, one was an arteriosclerotic man of 70 with a hypochromic anæmia and bundle branch block; the second, a man of 33, where, after a coronary thrombosis one year previously, the improvement followed ambulant treatment of his œdema by diuretics; and the third, a man with Addison's disease, whose blood pressure had risen from 110/60 to 150/90 after a desoxy-corticosterone acetate implant. These patients had little in common, but it is possible that improvement in cardiac function was not the chief cause of their better health.

The two cases, both with coronary occlusion, who had deteriorated, showed falls in V of 20 per cent and 75 per cent respectively. The first presented no definite clinical change, with a variable blood pressure, but the cardiographic pattern showed regression and another occlusive attack followed three days after the second tracing.

DISCUSSION

The principal value of the clinical electrocardiogram is to provide information on abnormalities of rhythm and on disturbances of conduction of the contractile impulse. It is with the object of supplementing this by a quantitative figure based on the total resultant electromotive force generated during ventricular systole that the above method is put forward. It is realized, in the first place, that this resultant force itself, the summation of an electrical system of vast complexity, bears no well-defined relationship to the capacity of the heart to do work, and further that one measures only that proportion of the total that can be derived from peripheral electrodes. The method is therefore an arbitrary one, to be judged from a practical standpoint.

Although there is wide personal variation in the normal heart, it appears to be exceptional

for the V value to fall below 10 mm. or to exceed 25 mm. in health. There is a much wider scatter in cases of heart disease, but it is clear that low values are in general associated with increased degrees of ventricular disease or embarrassment rather than the opposite.

If, therefore, V is found to alter during a patient's illness, the direction and extent of this change might be used to assess the severity of the disease as it affects the ventricular muscle, as a measure of progress and as a guide to prognosis. Further, a rising figure during recovery from an illness may permit a retrospective diagnosis of transient myocardial damage to be made where the standard tracing has shown no abnormality. The magnitude of the variations of V observed in changing clinical states encourages the belief that myocardial involvement may be recognized in this way in cases where failure is absent and where other clinical methods give no information.

Although the direction of the vector is not discussed in this paper, it may be mentioned again here that the combination of sagittal and frontal electrocardiograms enables the observer to fix in space the vector itself instead of simply a frontal projection of it. In this way "axis deviation" in the sagittal plane can be studied. This is of value in cases of ventricular preponderance, as anatomically the main bulks of the respective ventricles lie more in a fore-and-aft plane than transversely, and the sagittal axis is less likely to be disturbed by variations in build and diaphragmatic level.

Another incidental finding in this work was the occasional elucidation of tracings that showed very small deflections in the limb leads. These low-voltage curves were twice found to be due to the rotation of the vector away from the frontal plane, so that it lay almost at right angles to it, giving in the limb leads the equivalent of a foreshortened image. One such subject showed in all the limb leads the prolonged, low, polyphasic initial deflections often attributed to arborization block. His sagittal cardiogram showed broad, high, monophasic deflections whose measurements indicated that the electrical vector was of normal dimensions but pointed directly antero-posteriorly. This suggests an explanation of the high-voltage præcordial tracings often recorded in such cases.

Summary

A method of recording a sagittal electrocardiogram is described.

From the measurements of the initial ventricular deflections in this and the standard frontal electrocardiogram the magnitude and direction can be calculated of the vector quantity that represents the total electromotive force generated during ventricular systole.

The apparent magnitude of this vector in 50 normal subjects and 101 patients with heart disease is given, and the significance of the findings in various grades of cardiac disability is discussed.

The value is shown generally to rise or fall in accordance with clinical estimations of the functional capacity of the heart, where this undergoes change in the same patient.

Possible clinical applications of the method are suggested.

We wish to thank the many friends who have given their time to act as volunteers, the staff of St. Mary, Islington, Hospital (L.C.C.), where most of the work was done, for their kind co-operation, and especially Sister H. Pound for her valuable technical assistance in making the recordings.

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A CASE OF MYXOMA OF THE HEART

BY

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The following account of a case of cardiac myxoma is offered because of the rarity of British descriptions of this unusual condition.

A woman, aged 29, was admitted to Aberdeen Royal Infirmary on April 17, 1944, as a case of breathlessness of unknown origin for investigation. She had been a waitress for eight years and had been in good health until a year prior to admission. Since then she had suffered from breathlessness on walking, rendering impossible any additional exercise such as climbing stairs. She had associated palpitation and occasional spells of dizziness when trying to hurry. No other symptoms were complained of, and the degree of disability had not increased since its onset.

The patient was a healthy looking, well-coloured woman, afebrile, with a regular pulse varying between 68 and 92, and a blood pressure of 108/70. The apex beat of the heart was felt three and a half inches from the mid-line in the fifth left intercostal space. The mitral first sound was accentuated and followed by a high-pitched systolic murmur. The pulmonary second sound was also loud. No mitral diastolic murmur was heard, and none had been heard at the out-patient examination. The day after admission, however, a rough mitral presystolic murmur appeared and remained, the other cardiac findings being as before. Radiological examination showed definite enlargement of the left auricle, slight enlargement of the right auricle, doubtful enlargement of the right ventricle and none of the left. There were no signs of cardiac failure. Accordingly, but not without some misgivings, the condition was diagnosed as mitral stenosis, of rheumatic origin, and the patient was discharged on April 20, with advice to obtain lighter work.

On June 20, she was re-admitted with heart failure. She had rested in bed for three weeks after her discharge and had then become a sedentary worker, with a four-hour day. She had felt very breathless at work, and had experienced severe attacks of breathlessness when walking home. After five days she was forced to go to bed, where she remained, more or less constantly breathless at rest, and suffering a steady epigastric pain. About a week before re-admission, she became still more breathless, with paroxysmal nocturnal dyspnœa, following a prelude of vague lumbar and generalized pains, shivering, and feverishness.

She was distressed, cyanosed, and orthopnœic. The blood pressure was 110/84, the temperature normal, the pulse 112, regular but weaker in volume. The apex beat was now four and a half inches from the mid-line in the fifth space, and on percussion the heart appeared to be enlarged three-quarters of an inch to the right of the sternum. A well-marked rough mitral presystolic murmur and a mitral systolic murmur were present. The superficial neck veins were engorged up to the level of the angle of the jaw, the liver was palpably enlarged and tender, and œdema was present over the sacrum and in the legs; moist sounds were heard at the bases of the lungs. X-ray examination including fluoroscopy of the heart, undertaken with difficulty, showed enlargement of the left ventricle and of both auricles, especially the left, which displaced the œsophagus. An electrocardiogram showed normal P waves, low voltage of T I and T II, slight depression of S–T III, and a marked right axis deviation. Treatment with rest, light diet, restricted fluids, digitalis, and mercurial diuretics, was instituted, but apart from a slowing of the heart to normal rate, little response was

FIG. 1.—Tumour in left auricle protruding through mitral valve: pedicle attached to interauricular septum: hypertrophy of right ventricle. Natural size.

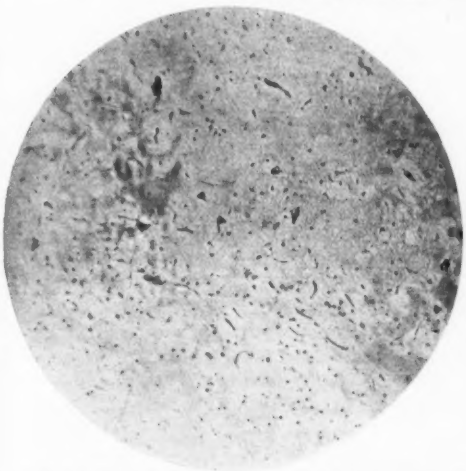

FIG. 2.—Field from tumour: abundant homogeneous matrix: scattered polymorphs and mononuclears among tumour cells. Magnification × 70.

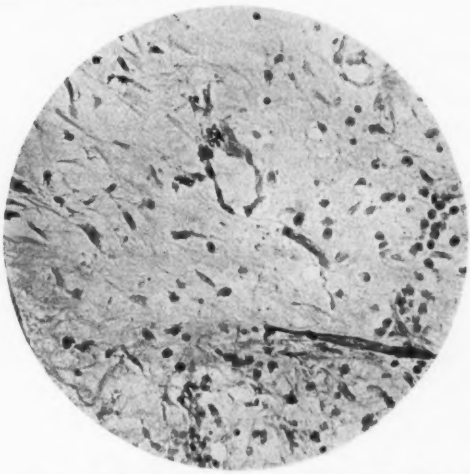

FIG. 3.—High-power view of tumour cells: thin-walled blood vessel in upper part of field. Magnification × 140.

obtained. The patient became steadily weaker, the liver increased in size with accompanying jaundice and a distressing hiccough, and infarction occurred in the right lung; finally renal secretion diminished to nothing, the blood urea level rose to 180 mg. per 100 c.c., and death took place in coma on July 6.

Examined post-mortem, the body was that of a well-developed well-nourished young female subject, showing gross œdema of the ankles and legs, marked lividity of the lips and ears and extremities, and faint icterus of the skin and conjunctivæ. The pericardial sac contained 100 c.c. of straw-coloured transudate. The heart, much enlarged, weighed 380 grams. The lumen of the dilated left auricle was almost filled by a smooth rounded tumour, 7·5 cm. × 3·5 cm. × 3·5 cm., attached to the interauricular septum; the base of the attachment was approximately 2 cm. in diameter. The tumour protruded through the mitral orifice (Fig. 1). Its cut surface was greenish semi-translucent and glistening, suggestive of myxoma, with occasional small hæmorrhages. There was no hypertrophy or dilatation of the left ventricle. The right ventricle was dilated and its hypertrophied wall was almost as thick as that of the left; the tricuspid ring was dilated. A small ante-mortem thrombus adhered to the endocardium of the right auricular appendage. The coronary arteries and the cusps of all valves appeared normal. The lungs, liver, spleen, kidneys, and other organs showed chronic venous congestion; a small recent infarct was present in the lower lobe of the right lung and another in the middle lobe.

Microscopically, the tumour was a myxoma, comprising spheroidal, spindle, and stellate cells with a very abundant homogeneous matrix (Fig. 2), staining bright pink with Southgate's mucicarmine; it possessed very numerous capillary vascular channels enclosed by a single or double layer of elongated endothelial cells (Fig. 3); occasional foci of hæmorrhage both recent and old were noted; numerous leucocytes, both mononuclear and polymorphonuclear, were dispersed through the matrix of the growth.

Summary

Cardiac myxoma was succinctly reviewed by Fawcett and Ward in 1939 and commented on by Thompson in 1944. This case belongs to the group in which, clinically, the resemblance to the picture of mitral stenosis is strong but the differences are significant. Thus the mitral diastolic murmur was inconstant, a previous history of rheumatism was lacking, the whole symptomatic course of the illness lasted less than 15 months, and the terminal heart failure developed rapidly and relentlessly, uninfluenced by treatment.

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PAROXYSMAL TACHYCARDIA AND 2 : 1 HEART BLOCK

BY

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Received June 21, 1945

Recent work of William Evans (1944), demonstrating with chest leads that many cases of paroxysmal tachycardia have a faster auricular rate with 2 : 1 heart block and so resemble auricular flutter, demands a re-examination of our views of paroxysmal tachycardia. Evans has shown that chest leads, and in particular CR_1, are the best method of detecting the form of auricular activity, and in view of this it may seem unwise to discuss the subject further when the material available is only the standard leads.

It is, however, possible to detect some signs of 2 : 1 block in nearly half of Evans' cases using the limb lead only (see p. 194); and it may be some time before adequate evidence with chest leads can be obtained as it is easier to make the diagnosis of, than to obtain graphic records of paroxysmal tachycardia. Meanwhile, it is important that well-established clinical facts should not be lost sight of or obscured, and that until a final classification is accepted, steps should be taken to minimize any confusion that may arise among those less familiar with and less regularly concerned with cardiographic interpretation.

The present paper deals with paroxysmal auricular (or supraventricular) tachycardia where electrocardiograms of the paroxysms were available. There is enough evidence in these records to show that 2 : 1 A-V block in paroxysmal tachycardia has often been missed and is more common than has been thought, but enough to show that it is far from being the rule. Nor does the finding of 2 : 1 block in auricular tachycardia prove that the mechanism is the same as in auricular flutter with 2 : 1 block. Evans' remarks about the rate in attacks are specially discussed: there does not appear to be any exact dividing line separating the two varieties of paroxysms according to rate. This paper is based on a study of 66 cases. In the paper of Campbell and Elliott (1939) there were 42 cases with cardiograms, but 8 of these were paroxysmal ventricular tachycardia. The remaining 34 cardiograms (taken between 1925–32) and 32 others (taken between 1933–39) have been carefully re-examined for possible evidence of 2 : 1 block. The last 32 were not a consecutive series, but their selection depended entirely on which records I have been able to find under war-time conditions after the destruction of some plates by enemy action. Unlike Evans, I have not included cases diagnosed as paroxysmal auricular flutter, and 17 examples of this are discussed separately.

I have, however, realized more strongly than ever that there are cardiograms where it is not easy to make the diagnosis between paroxysmal auricular tachycardia and paroxysmal auricular flutter (Fig. 4B, 7, 9, and 11). In the course of writing this paper two cases (see Fig. 12) have been removed from the latter to the former group.

In these 66 cases 22 provide some evidence of 2 : 1 block—10 clearly and 12 much more doubtfully—and 13 provide evidence against it. During the last few months I have not been able to get a record with chest leads of a paroxysm in any of these 13 patients, but in many of them the signs of auricular activity are so clear and the spacing of the different waves so arranged that it seems impossible that these could be 2 : 1 block. In the remaining 31 (half the total) I have not been able to see any evidence for 2 : 1 block, but the mere fact that it could be hidden and is not impossible in so many cases may be held to support Evans' view that it is common, and may help to explain why it has not been recognized more often.

TABLE I

CASES OF PAROXYSMAL TACHYCARDIA WITH OR WITHOUT EVIDENCE OF 2 : 1 BLOCK

	With evidence of 2 : 1 block: favouring Evans theory		With " no evidence "	With evidence against the presence of 2 : 1 block
	+	(+)		
Series A (published) (34 cases) ..	4	6	19	5
Series B (unpublished) (32 cases) ..	6	6	12	8
Total (66 cases)	22		31	13

The differentiation of these three groups does not depend merely on the rate. In those with signs of 2 : 1 block the rate averaged 171 and varied between 144–193 (excluding the slowest and the two fastest cases). In those with evidence against 2 : 1 block the rate averaged 157 and varied between 140–176 (excluding the two slowest and the two fastest). In those without evidence either way the average rate was a little faster, 187, and twelve had rates between 200 and 240, but the remaining nineteen had rates between 145–190, the same as in the other groups. So the only conclusion that can be drawn is that if the rate is over 200 it is more difficult to see in the limb leads if there is or is not any evidence of 2 : 1 block.

PAROXYSMAL TACHYCARDIA WITH EVIDENCE OF 2 : 1 A-V BLOCK

Four of the 34 cases of my published series and 6 of the 32 of the second series provide fairly good evidence of hidden 2 : 1 block of the type described by Evans (1944) even without the study of chest leads.

The first (Fig. 6, Campbell and Elliott, 1939) has a deeper and wider S wave in lead II in paroxysms than in normal rhythm and this lies exactly half-way between the inverted P waves, showing its real nature. This is well shown in three separate paroxysms (Fig. 1A, all lead II) but is more difficult to see in leads I and III (Fig. 1B) although there is again in lead I the wider R wave without this clearly having the same significance.

In the second (Fig. 2) the 2 : 1 block (which was missed previously) is best shown in leads I and II where parts of the alternate missing P waves have been marked in on the left of the figure. In both leads I and II it is the curved upstroke of R (occurring exactly half-way between the two easily visible P waves) that represents the fusion of a hidden P wave and an ordinary R wave.

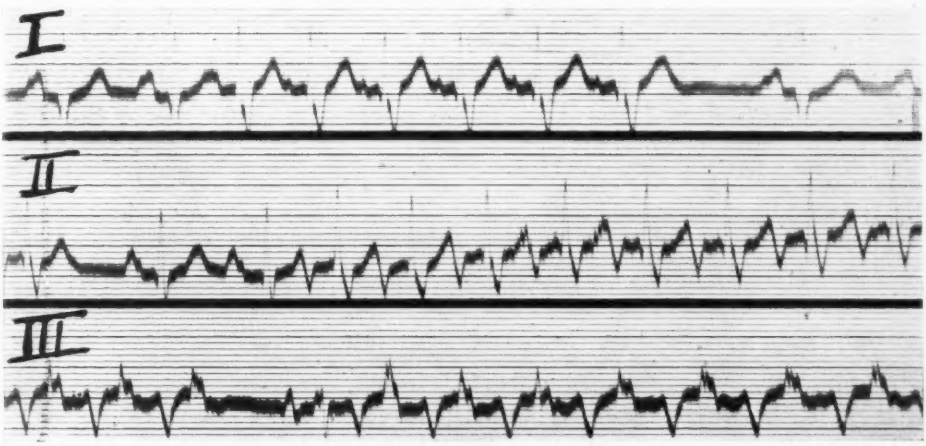
The third (Fig. 3) is perhaps less convincing, but especially in lead II of one paroxysm and in lead III of another there seems clear evidence of a small wave at a rate double that of the ventricle. None of these three look like the ordinary curves of 2 : 1 flutter.

The fourth (Fig. 5, Campbell and Elliott, 1939) is best shown in the small wave coming immediately after S in lead II and in the peak just after S in lead III, both these features being absent from the accompanying record of normal rhythm and being placed just half-way between the more obvious evidence of auricular activity. This patient, aged 57 when his paroxysms started, developed established auricular fibrillation 6 years later: it is possible that his paroxysms were flutter with very poorly marked auricular waves.

The fifth case has two very different types of paroxysms in 1934 and in 1937. The former (Fig. 4A) had no very good evidence of 2 : 1 block though the points that make me think it is present have been marked. (If those who are not convinced would set their dividers for exactly half the distance between successive R waves, I think they will be surprised at how often this shorter distance seems to fit exactly on to some rather small waves that had previously seemed obscure.) The later attacks (Fig. 4B) seem to have rather clearer evidence of 2 : 1 block though the auricular waves are very minute. This is the sort of case where the chest leads would probably show the auricular activity more clearly. It is also a case where the possibility of flutter with very small auricular excursions must be considered.

The sixth case (Fig. 5) is one where I had many records taken over some years, both of paroxysms and of normal rhythm. In normal rhythm the upstroke of R II is generally notched with a rather short P–R interval and the downstroke is always sharp: in paroxysms the downstroke of R is always notched and this is exactly half-way between the most prominent wave (probably P) between the QRS waves.

A



B

FIG. 1.—Paroxysmal auricular (? high nodal) tachycardia with 2: 1 block (A, 300; V, 150) from a boy with a heart that was otherwise normal, who had frequent short paroxysms during four years' observations. Case 2.

(A) Lead II only. Deeper and wider S waves are seen in all three paroxysms exactly half-way between the inverted P waves. (B) Standard leads. The same change is readily seen in lead II; in leads I and III it can, I think, be seen but would have been more difficult to demonstrate without lead II. This and the other figures have been reduced to about 5/6ths.

The seventh (Fig. 6) is rather different. That there is some auricular activity twice as fast as the ventricular seems very obvious in any of the three standard leads, but it had not been noticed by me though perhaps it would have been by many readers. (I had not studied this record for publication in my previous series but have always been interested in all my records of paroxysmal tachycardia.) The wide notched P wave following QRS had been passed as a wide notched QRS. The P wave in normal rhythm is less notched but it is wide and the P–R interval is prolonged so 2 : 1 block is less unexpected.

The eighth (Fig. 7) and ninth are similar and without making a firm diagnosis I had thought of paroxysmal flutter with 2 : 1 block but had decided on paroxysmal tachycardia because of the shape of the curve of auricular activity. Some may think the first diagnosis was correct as there is little of the curve on the iso-electric level.

FIG. 2.—Paroxysmal auricular (? high nodal) tachycardia with 2 : 1 block (A, 300; V, 150) from a woman, aged 26–50, with mitral stenosis. Her attacks lasted up to 9 hours and came about once a month. Case 3. The second wave is partly hidden by QRS but its suspected shape has been inked in and marked with an arrow on the left of the figure.

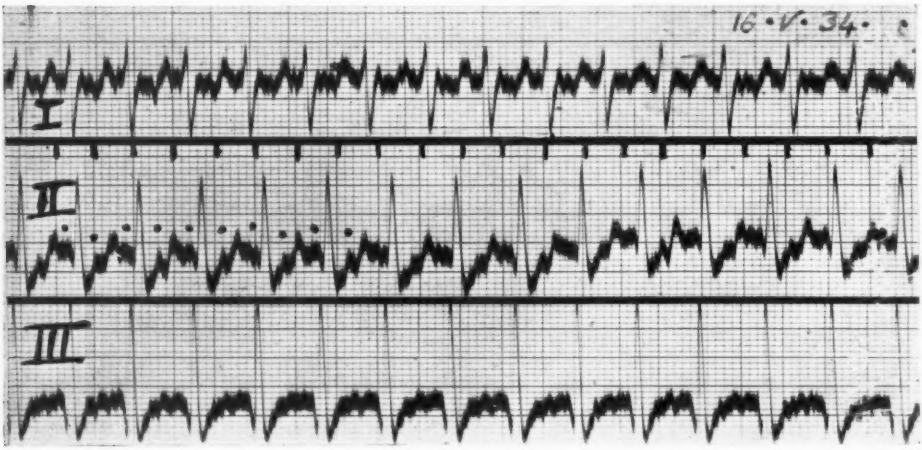


FIG. 3.—Paroxysmal supraventricular tachycardia with 2 : 1 block (A, 396; V, 198). From a woman, aged 27, with mitral stenosis who was under observation 9 years with attacks lasting from 6–48 hours. Case 84. The suspected P waves have been marked with a dot in lead II.

The tenth (Fig. 8) was (I now think wrongly) classified as paroxysmal flutter mainly because he showed at times 2 : 1 and at other times 1 : 1 block. Diagnosed clinically as paroxysmal tachycardia the first record of an attack shows 2 : 1 block (A, 222; V, 111; Fig. 8A). Although the auricular waves were not the shape of flutter I decided that the presence of block indicated this diagnosis. A few days later Fig. 8B was obtained without 2 : 1 block (A, 182; V, 182). This was certainly slow for 1 : 1 flutter which I thought it must be on the evidence of Fig. 8A, and alone it would certainly have been diagnosed as paroxysmal tachycardia.

Incidentally Fig. 8B disproves Evans' suggestion that all cases have 2 : 1 block. If 2 : 1 block is present but missed in this record, then 4 : 1 block should be present in Fig. 8A; this is obviously not so, as the curves indicating auricular activity could not be seen more clearly than they are in the standard leads.

FIG. 4.—Paroxysmal supraventricular tachycardia with 2 : 1 block from a man, aged 68, with a large heart and high blood pressure, with attacks of increasing frequency lasting up to 7 days during the last 4 years of his life.

(A) 16/7/34, leads II and III. A, 332; V, 166. (B) 24/12/37, leads II and III. A, 342; V, 171. This might be flutter with 2:1 block with very low voltage auricular curves. In both cases the suspected P waves have been marked with dots.

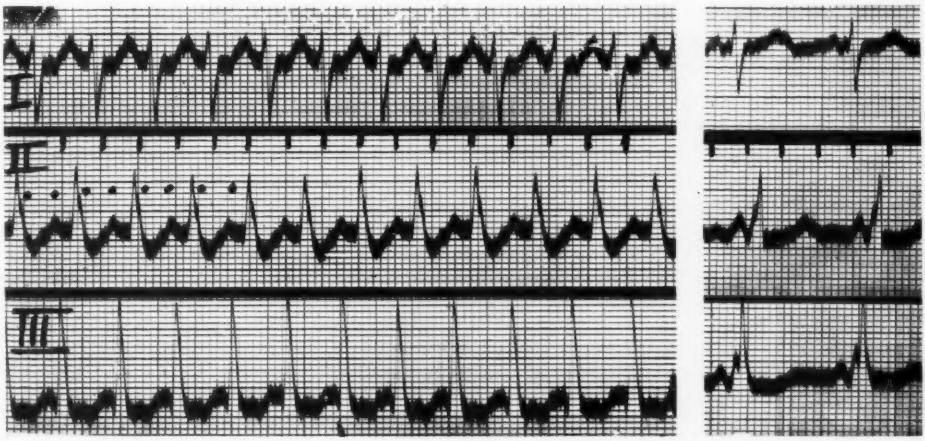


FIG. 5.—Paroxysmal supraventricular tachycardia with 2 : 1 block from a woman, aged 46, whose heart was otherwise normal. Attacks had been present for 25 years and lasted up to 48 hours.

On the right, normal rhythm. On the left, paroxysmal tachycardia (A, 386; V, 193), with the intervening P wave notching the downstroke of R in lead II and to a lesser extent in lead III.

I was reminded by these last records of an earlier one that I had put away not labelled more precisely than auricular tachycardia with 2 : 1 and 1 : 1 block (Fig. 9). I had not diagnosed paroxysmal tachycardia because the attacks were so long that it was almost if not quite the dominant rhythm during the last months of his life; but the marked waves favour this diagnosis, though the general shape of the curve resembles flutter. I have not included this case in either group.

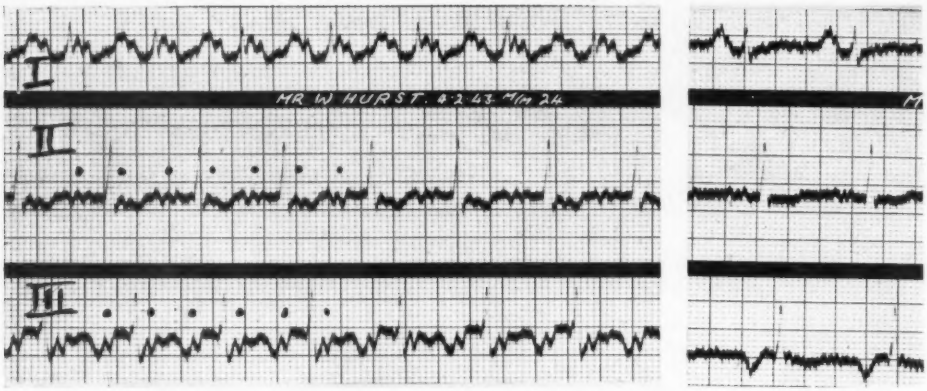


FIG. 6.—Paroxysmal auricular tachycardia with 2 : 1 block (A, 228; V, 114) from a man, aged 29, with mitral stenosis. His attacks generally lasted about 1–6 hours and had been present several years.

On the right, normal rhythm, rate 82. On the left, a paroxysm. The P waves are large and notched, even more than in the record of normal rhythm, and this produces an unusual and curious appearance of the record. It is also unusual in that the 2 : 1 block is most easily seen in leads I and III.

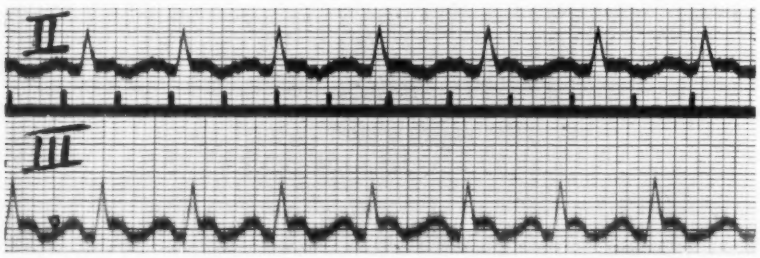


FIG. 7.—Paroxysmal auricular tachycardia with 2 : 1 block (A, 338; V, 169) from a woman, aged 50, with hyperthyroidism, and frequent paroxysms, generally lasting a few hours.

The 2 : 1 block is more obvious than in many records and paroxysmal flutter with 2 : 1 block was thought a possible diagnosis. The shape of the auricular curves (here and in Fig. 9) is somewhat like flutter, but on the whole the shape was thought to be more against than in favour of flutter.

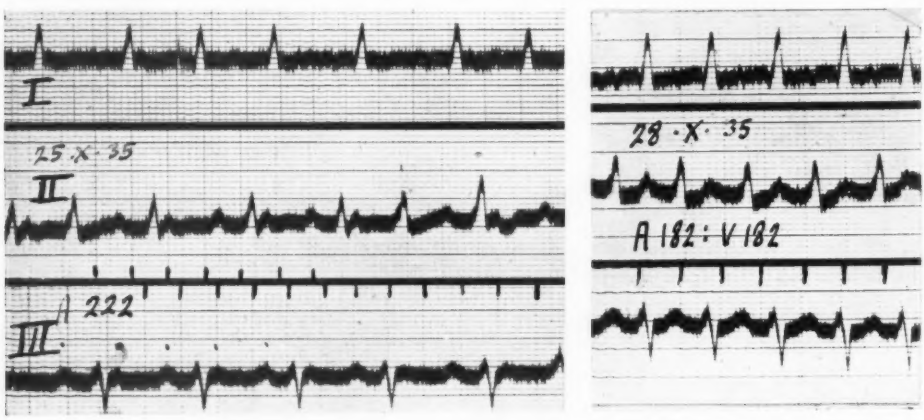


FIG. 8.—Paroxysmal auricular tachycardia with and without 2 : 1 A-V block, from a man of 44, who died with acute pericarditis and possibly syphilitic myocarditis after 18 months with paroxysms, generally lasting one or two hours.

(A) With 2 : 1 block. A, 222; V, 111. (B) Without 2 : 1 block. A, 182 V, 182.

Fig. 8 (B) proves that paroxysmal tachycardia occurs without hidden 2 : 1 block, because if 2 : 1 block was present but hidden here, 4 : 1 block would be present in Fig. 8 (A), which is obviously not the case.

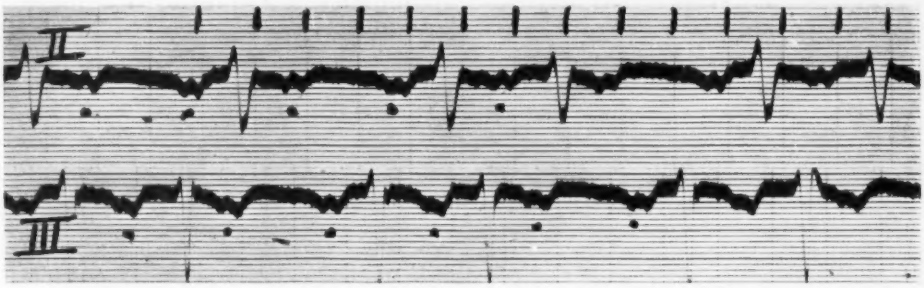


FIG. 9.—Irregular block (1 : 1 and 2 : 1) in auricular tachycardia from a man, aged 65, with myocardial disease. The case was not diagnosed as paroxysmal tachycardia, because of the block (now admitted to be an inadequate reason) and because the tachycardia was present for nearly or quite as much time as the normal rhythm. Lead II and III only.

The 12 that provide some slight evidence of 2 : 1 block need not be detailed but Fig. 10, 11, and 12 are given as examples. If the earlier 10 cases have not succeeded in convincing the reader that 2 : 1 block occurs but has been overlooked, these less striking ones will not do so: in any case a final decision as to how common the different types are will have to be reached after more detailed studies of unselected series making use of chest leads.

Fig. 10 is from a woman of 39 who had had frequent paroxysms for four years. She was obese and had a severe microcytic anæmia (Hb. 36 per cent but had been raised to 55 per cent with iron). She died from a pulmonary embolism from extensive venous thrombosis in both iliac veins. Death was during the second day of an attack but there had been other longer attacks. It is only in lead III as marked that there seemed to be some evidence of 2 : 1 block.

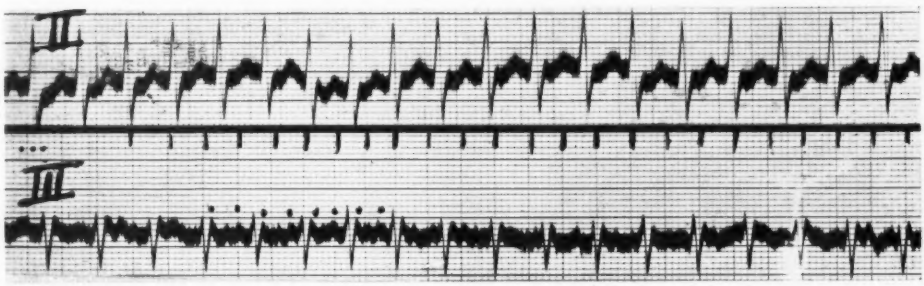


FIG. 10.—Paroxysmal supraventricular tachycardia with possible 2 : 1 block. Ventricular rate 200 (see text). Leads II and III only.

Fig. 11 has perhaps a little more evidence of 2 : 1 block as marked in leads II and III. The only known paroxysm followed a gastrectomy for a fibro-sarcoma of the stomach in a man of 61; the rhythm changed to fibrillation after seven days and then to normal rhythm with digitalization.

Fig. 12 shows a paroxysm—the only known one in a woman, aged 48, who had been under observation for twelve years with bradycardia and cardiac enlargement of unknown origin. She was in hospital at the time with bronchitis and threatened left ventricular failure. Generally she had left ventricular preponderance with rather wide QRS waves but not the picture of bundle branch block as during the attack. This was a record first diagnosed as paroxysmal tachycardia, then (on evidence of lead II) as paroxysmal flutter with 2 : 1 block, and finally again as probable paroxysmal tachycardia.

Fig. 13 (here) and Fig. 4 and 18 (Campbell and Elliott, *loc. cit.*) may be taken as examples of curves I have classified as " no evidence." I can find nothing to suggest that there is 2 : 1 block but the main waves R and T or R and P are so spaced that they could hide such evidence if it was present.

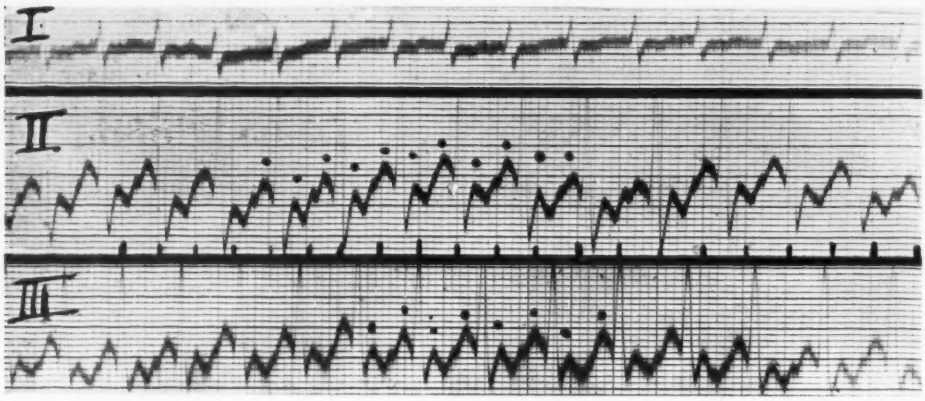


FIG. 11.—Paroxysmal supraventricular tachycardia with possible 2 : 1 block. Ventricular rate 166 (see text). Owing to the shape of the curves of auricular activity, it is more difficult to exclude auricular flutter with 2: 1 block in this case.

FIG. 12.—Paroxysmal tachycardia, ventricular rate 148 (see text).
It is thought to be paroxysmal auricular tachycardia with bundle branch block and 2 : 1 block; but a diagnosis of paroxysmal ventricular tachycardia or of paroxysmal flutter with 2 : 1 block (see lead II) could be made. This curve illustrates the difficulty of decisive diagnosis in such cases without other experimental observations.

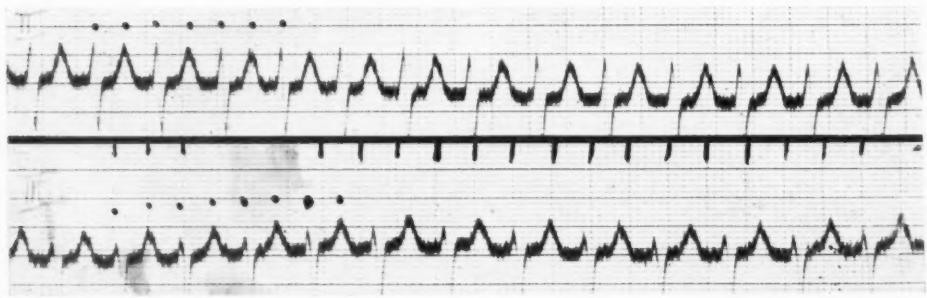


FIG. 13.—Paroxysmal supraventricular tachycardia where there is no direct evidence of 2 : 1 A-V block, but where it can not be excluded, as indicated by the dots. Ventricular rate 166. Leads II and III only.
From a man, aged 49, whose heart was otherwise normal. Paroxysms had been present for 5 years and did not generally last more than 2 hours.

Fig. 13 is from a patient whose attacks were clinically ordinary paroxysmal tachycardia: there is no positive evidence of 2 : 1 block but the sharp tip of the T wave is so exactly halfway between the rather broad R that P waves might be hidden at one or both of these points. Half of all my cases (31 of 66) belonged to this group.

Paroxysmal Tachycardia without 2 :1 Block

In his series Evans recorded no such cases, but they appear to be fairly common—13 of the 66 cases. In these the curves of auricular activity are easily seen, and at the point halfway between these waves there is a level or nearly level iso-electric period in which it should be easy to see the second auricular wave were it present. Fig. 14 (Fig. 7 of Campbell and Elliott) is perhaps the most striking example.

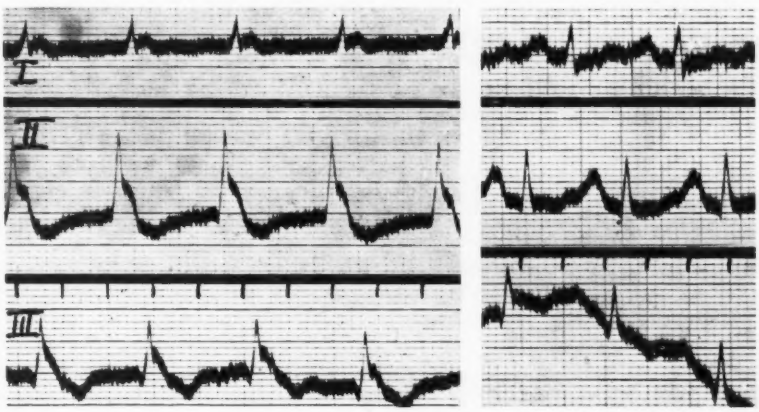


Fig. 14.—Paroxysma nodal tachycardia, rate 125, without 2 : 1 block. On the right normal rhythm From a woman, aged 27, with mitral stenosis (Case 87). Attacks had been present for 6 years and generally lasted less than an hour.

The ending of the large P wave is seen just on the downstroke of R, especially in lead II, and there could not be 2 : 1 block as such a large wave could not be missed elsewhere in the record.

Three other examples of different types of supraventricular paroxysmal tachycardia are illustrated. In Fig. 15 the P–R interval is normal in the paroxysm in lead II but the P wave is fairly deeply inverted—the type that I have called " high " nodel. A second P wave, if it

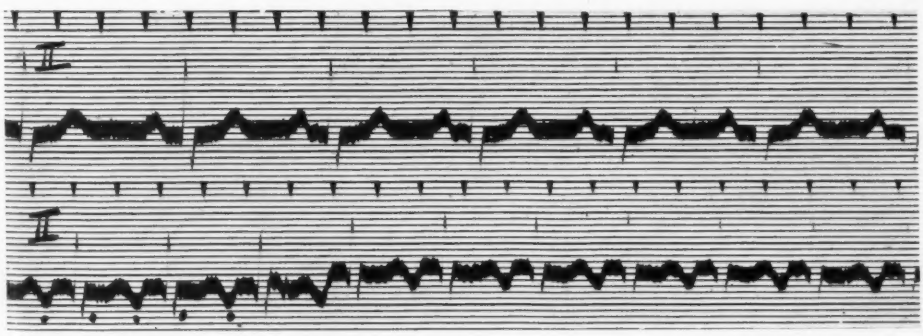


Fig. 15.—Paroxysmal " high nodal " tachycardia without 2 : 1 A-V block (below); and normal rhythm (above). From a woman, aged 34, with frequent short attacks whose heart was otherwise normal. Case 22. Lead II only.

The spacing is such that a second inverted P wave would be easily visible after QRS, were it present.

were present, would be easily seen in the smooth iso-electric S–T period shortly after S (marked with a dot).

Fig. 16 has an inverted P wave shortly after QRS—a typical example of nodal tachycardia. If a second P wave were present it should be easily seen in the level period just before QRS

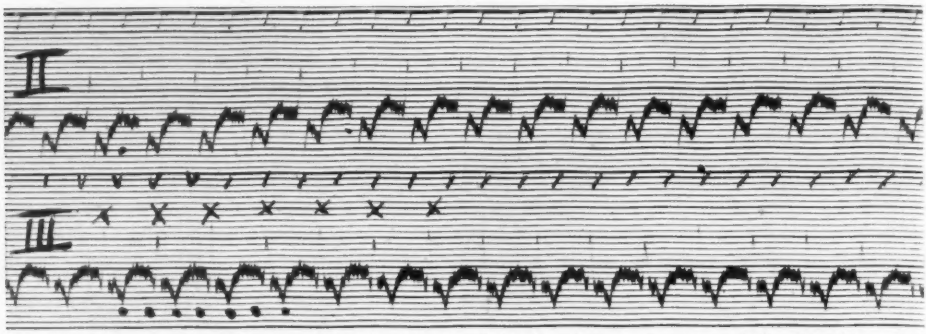


FIG. 16.—Paroxysmal nodal tachycardia without 2 : 1 A-V block. From a woman, aged 53, with a heart that was otherwise normal and frequent paroxysms lasting up to half an hour over a period of 36 years. Case 42. Leads II and III only.

The spacing is such that a second inverted P wave would be easily seen before QRS (as marked with dots), were it present.

in either lead II or III, and as there is no deformity there it is certain that 2 : 1 block is not present in this case either. If the rate happened to be a little faster the hypothetical P wave might be present but hidden in the start of QRS and this would place the case among those I have classified as " no evidence."

Fig. 17 is auricular tachycardia at two slightly different rates so that the P wave is some-

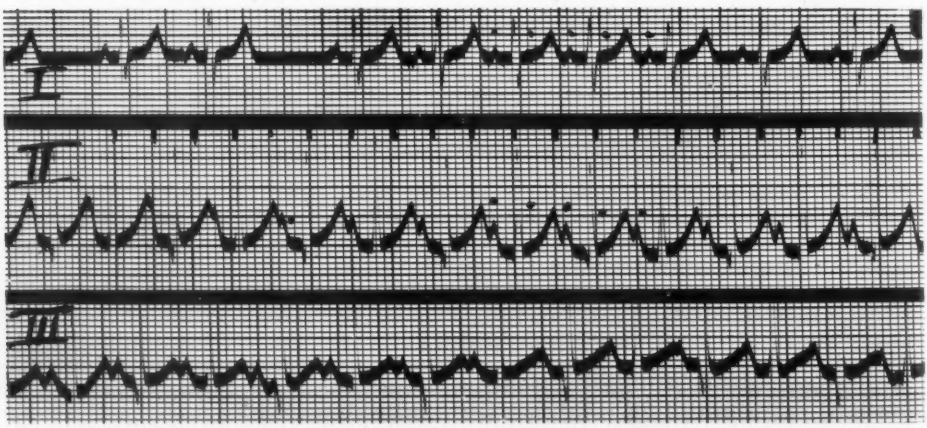


FIG. 17.—Paroxysmal auricular tachycardia without 2 : 1 A-V block. From a small child with a congenital heart (probably a ventricular septal defect with some degree of pulmonary stenosis) who had frequent paroxysms generally lasting for hours and died about a year later with pneumonia.

The spacing is such that a second upright P wave would be easily seen after QRS (as marked with dots), were it present.

times almost or quite hidden in the downstroke of the preceding T wave (rates 150 and 166). Again if a second P wave were present it should be clearly seen and could not be missed in the smooth slowly rising period shortly after S (marked with a dot).

Szekely (1944) reported some chest lead cardiograms of paroxysmal tachycardia which help to prove that 2: 1 block is not always present (his Fig. 1 and 2A). Fig. 2A is specially conclusive because Fig. 2B shows that 2 : 1 block could occur and was easy to detect in this patient (compare my Fig. 8).

It seems, therefore, that in some records of paroxysmal tachycardia, more than one-quarter, there is, even in the standard leads, some evidence of auricular activity at twice the expected rate with 2 : 1 A-V block. It is, however, equally clear that in other records, nearly one-quarter, there is decisive evidence that no A-V block is present. About the remaining half it is not possible to express an opinion without further study using chest leads.

Discussion of Evans' Cases

At first sight the findings of 2 : 1 A-V block in all of Evans' 27 consecutive cases is almost conclusive evidence that such block is present in all or nearly all cases of paroxysmal tachycardia. But examination of the cases makes this rather less certain, partly because he includes cases of flutter and partly because many of his cases are of a rather unusual type so that the series cannot be regarded as representative of paroxysmal tachycardia as a whole. Evans has kindly lent me the records of 11 of the unpublished cases so that 26 of the 27 can be discussed.

Case 6 (his Fig. 7) is certainly auricular flutter, sometimes with 2 : 1 and sometimes with 3 : 1 block. Evans agrees that by the criteria he has chosen for the selection of these cases paroxysmal flutter would be included. This also applies to his Cases 15 and 26. Case 26 is of special interest because the first record is orthodox flutter with 2 : 1 block (A, 218; V, 109) and the second shows a quite different picture at a rate of 217. Seeing this alone I should call it paroxysmal ventricular tachycardia; with the previous record it seems more like 1 : 1 flutter with bundle branch block owing to the more rapid rate. Evans regards it as 2 : 1 block in paroxysmal tachycardia (A, 434; V, 217) but his two auricular waves might be the first notch of the ventricular complex and a retrograde P wave on the downstroke of R: if he is correct it is hard to explain why there is 2 : 1 block at such different auricular rates as 434 and 218, the former showing that the ventricle is quite capable of responding at a rate of 217.

Cases 5, 9, and 14 (his Fig. 6, 11, and 14) might be regarded as flutter on the standard cardiograms. With the knowledge I have gained from Evans paper I have no difficulty in finding evidence of 2 : 1 block in leads I, II, or III (and actually it is clearer in III than in CR_1, for Fig. 11). The first two had mitral stenosis and certainly the second had not typical paroxysmal tachycardia, but the third was a woman who was otherwise healthy, with typical paroxysmal tachycardia.

Cases 1 and 2 (his Fig. 3 and 4) have not got a regular rhythm in their attacks. Even in the standard leads of Case 1, I can now find the evidence of block but it is clearer in CR_1. In Case 2, no such evidence can be found without the help of CR_1. Cases 1 and 2 on the history available do not appear typical cases of paroxysmal tachycardia especially because the arrhythmia was converted to fibrillation with digitalis in each case.

This still leaves 18 cases, including 9 of those illustrated, where the cardiograms would certainly have been passed by everyone as paroxysmal tachycardia. In 11 of them the history also is of classical paroxysmal tachycardia, but in the other 7 some question might be raised: in Case 3 because " latterly the attacks had lasted for some months," in Case 4 because they occurred during a terminal heart failure with broncho-pneumonia and were changed to fibrillation with quinidine (once); in Cases 7 and 16 because the attacks only came in the terminal stages of mitral stenosis and once (in Case 7) the rhythm was changed to fibrillation by digitalis; and in Cases 18, 19, and 23 because they occurred after cardiac infarction and in Case 18 were changed to fibrillation by digitalis; Cases 19 and 23 died within a short period.

It is, of course, true that paroxysmal tachycardia may occur for the first time in the late stages of heart failure or after cardiac infarction, and may at times change to fibrillation under the influence of digitalis; but both these events are more common with auricular flutter, and therefore such cases are not the best ones for evidence of the characteristic and common behaviour of paroxysmal tachycardia.

Even so, if one is hypercritical and rules out every case where the diagnosis might be questioned on cardiographic or more doubtfully on clinical grounds there are still 11 cases of classical paroxysmal tachycardia. In all of these 11 (except perhaps in Case 22 (his Fig. 15)

and Cases 17 and 20, not illustrated, where the evidence still seems to me inconclusive) there was certainly 2 : 1 A-V block.

For comparison with my own figures I have examined Evans standard limb lead cardiograms for signs of 2 : 1 block in the 20 cases, including 11 with published cardiograms, but excluding the 6 that are or might be flutter. In 9 there seems to be no doubt that 2 : 1 block can be demonstrated (his Fig. 3, 8, 9, 10, 13, and 21, and 3 unpublished); in 11 I should still have to mark them as " no evidence ": none are examples of the records that seem to me against accepting his view as the rule for all cases of paroxysmal tachycardia.

That, even now after familiarizing myself with the slighter indications of 2 : 1 block, I can only discover evidence of its presence in less than half the cases shows how essential a lead such as CR_1 is in assessing auricular activity in paroxysmal tachycardia.

Other Cases with 2 : 1 Block

Most other workers who have found 2 : 1 block have reported only one or two cases and therefore do no more than prove that 2 : 1 block does occur, but two papers deal with a larger number of cases and must be considered in more detail.

Barker, Wilson, Johnston, and Wishart (1943) have reviewed 35 cases of paroxysmal auricular tachycardia with A-V block, generally 2 : 1, 18 of their own and 17 that had been reported by others. They found that these attacks differed in certain ways from ordinary paroxysmal tachycardia. The attacks lasted longer, in more than half the patients for two days or more and sometimes for 26, 60, and 94 days. The disability caused by the attacks also seemed to be greater but as this would probably be diminished by the presence of 2 :1 block the explanation may be the longer attacks and the relatively high proportion with organic heart disease. Full doses of digitalis often restored normal rhythm and quinidine also did so but less often. Pressure on the carotid sinus, mecholyl, and acetylcholine were only successful in stopping attacks in one case.

Barker *et al.* stress the value of præcordial or œsophageal leads as in some cases the auricular deflections are small or not readily apparent in the standard limb leads. They emphasize that all the curves are quite different from those of auricular flutter, in that the auricular waves are separated by periods of electrical quiescence with the curve at rest on the base line. They conclude that paroxysmal auricular tachycardia with A-V block resembles auricular flutter in many respects but differs from it in some important particulars.

In a further paper Barker, Wilson, and Johnston (1943) discuss the arguments for circus rhythm as the mechanism of paroxysmal auricular tachycardia, but this paper is less pertinent to the present discussion: they suggest that the circus movement must have special features and this may be because its circulation path includes either the S-A or A-V node. Decherd *et al.* (1944 and 1945), however, adduced arguments against the rhythm being due to a circus movement.

Decherd, Herrmann, and Schwab (1943) have described 38 cases of paroxysmal supraventricular tachycardia with some degree of partial A-V block: they were selected from 102 cases of paroxysmal tachycardia and so formed a high proportion. This group of cases, as they themselves emphasize, was very unlike an ordinary group with paroxysmal tachycardia. Of the 38 cases, 55 per cent died during the period in hospital when their paroxysm with block was observed. In 35 of the 38 congestive heart failure was present before the appearance of the paroxysmal tachycardia with A-V block, 80 per cent having hypertensive or arteriosclerotic heart disease. Only 7 patients had not received digitalis and 23 had " an obvious overdosage of digitalis." In 25 digitalis medication preceeded and may have precipitated the tachycardia. Aminophylline had been given intravenously to 7 cases shortly before the attack.

Only 2 of the 38 cases had hearts that were otherwise normal and of these one had received a moderate, and the other an excessive, amount of digitalis. The ætiological factors were, therefore, very unlike that generally found in a random sample of cases of paroxysmal tachycardia. They were, in fact, nearer in many ways to the ætiological factors found with paroxysmal ventricular tachycardia. They also resembled the conditions under which partial

heart block with dropped beats occurs in patients without paroxysmal tachycardia (Campbell, 1943)—digitalis medication, sometimes in excessive doses, and infection, and often the two combined.

Decherd *et al.* emphasize that we do not possess absolute criteria for the sharp differentiation of auricular tachycardia and flutter.

Finally the 2 : 1 block found by Decherd *et al.* and by Barker *et al.* is of a different type from that of Evans. Evans' cases had ventricular rates that were normal for paroxysmal tachycardia and auricular rates twice as fast as this. The other reported cases had auricular rates that were normal for paroxysmal tachycardia and slower ventricular rates—generally half as fast as the auricular rate. Thus, in the cases of Barker *et al.* with 2 : 1 block the auricular rate averaged 189 (most cases having rates between 160 and 220) and the ventricular rate half of this. And in the cases of Decherd *et al.* the auricular rate averaged 192, and was generally between 166 and 250, and the ventricular rate was half this. In the cases of Evans, on the other hand, the ventricular rate was normal, generally between 130–250, and he suggests that the auricular rate was twice as fast as this. These data are summarized in Table II.

TABLE II

HEART RATES IN PAROXYSMAL TACHYCARDIA

Author	Auricle	Ventricle
Barket *et al.*	160–220 (average 189)	80–110
Decherd *et al.*	166–250 (average 192)	83–125
Campbell	140–240 * (average 178)	140–240
Price (1941)	120–250 (usual 160–200)	120–250
Evans	260–500 *	130–250

On the other hand, the few cases of Brown (1936) appear to have been of the same type as those described by Evans, as he thought these were 2 : 1 A-V block with auricular rates of 300 and 428.

Before discussing the subject more generally, certain conclusions from a short series of cases of paroxysmal auricular flutter will be given.

PAROXYSMAL AURICULAR FLUTTER

Under the same conditions that I have collected 66 cases of paroxysmal tachycardia I have collected 17 cases of paroxysmal auricular flutter, in each instance with electrocardiographic evidence of the attack. Those cases where all the paroxysms showed an irregular rhythm simulating fibrillation and possibly some where paroxysms occurred only for a short time before flutter became established have been excluded.

The whole clinical picture of these patients is so different from paroxysmal tachycardia that even if it was proved that the underlying mechanism of both abnormal rhythms were the same or similar, some other explanation of the different clinical pictures would be needed.

Of the 17 cases, 12 were men and 5 were women. It has generally been found that flutter is more common in men, but that paroxysmal tachycardia has about the same incidence in both sexes. The age incidence was spread from 30–74, but the only two cases under 40 had rheumatic mitral disease. Even including them, the average age *when the attacks started* was 54 and the maximum incidence was between 55–59 years of age. The age distribution of the cases if shown below, where it is contrasted with the age incidence of paroxysmal tachycardia.

TABLE III

AGE INCIDENCE OF PAROXYSMAL FLUTTER AND OF PAROXYSMAL TACHYCARDIA (AT ONSET)

	Up to 9	10 to 19	20 to 29	30 to 39	40 to 49	50 to 59	60 to 69	70 and over
Paroxysmal auricular flutter: number of cases	—	—	—	2	2	8	4	1
Percentage	—	—	—	12	12	46	24	6
Paroxysmal tachycardia: percentage	7	16	31	22	12	8	4	—

* This over-simplifies the question because I agree with Evans that in some cases the true auricular rate is twice as fast as the apparent rate.

In paroxysmal flutter nearly all the cases started after 40 (88 per cent): in paroxysmal tachycardia most started before 40 (76 per cent).

There was an equally striking contrast in the ætiology. Half the cases with paroxysmal tachycardia were otherwise normal. Only three of those with paroxysmal flutter were without other evidence of heart disease and as these three were aged 55, 56, and 60 it is difficult to be sure that the hearts were really normal though the youngest of the three is still in good health 15 years later. The ætiological factors were as follows:

Congenital	.. ..	1	Coronary disease	.. ..	3	Chest diseases	3
Rheumatic	.. ..	2	High blood pressure	.. ..	2	Normal (aged 55, 56, and 60) ..	3
Thyrotoxic	.. ..	2	Heart failure	.. .. ..	1		

Equally striking was the difference in the length of time during which the attacks had been present before the patient came under observation. In paroxysmal tachycardia this period was often many years while in flutter it was generally not more than months or was clearly associated with some other development of the heart disease.

Only 5 of the cases had attacks that could be regarded as indistinguishable from ordinary paroxysmal tachycardia and in these they had been present for 2, 6, 9, 30, and 34 months—always less than three years. Possibly the first of these was an exception as he thought he had been cured after a year of paroxysmal tachycardia by Sir James Mackenzie, 22 years before: in the interval he had developed a blood pressure of 240/160 and had reached the age of 74.

In 4 others the attacks were generally irregular and often paroxysmal auricular fibrillation and it was only later that one or more attacks of flutter with regular A-V block were observed. The details were: paroxysms for 6 years, mostly irregular, later established auricular fibrillation; paroxysms for 4 years, nearly if not all irregular and frequently recorded as paroxysmal auricular fibrillation, good health with fewer paroxysms 12 years later; paroxysms for 5 years diagnosed as paroxysmal auricular fibrillation till a cardiogram showed auricular flutter with longish periods of regular 2 : 1 block (the irregular periods being a mixture of 2 : 1 and 1 : 1 were difficult to distinguish from fibrillation without the help of regular 2 : 1 periods); about equal numbers of paroxysms of flutter and fibrillation, both recorded, in an elderly woman with thyrotoxicosis.

In 4, the patients were already in hospital when the first attack occurred: with congestive failure; with cardiac infarction; with carcinoma of the bronchus; and with a pleural effusion. In 2 others the patient was so incapacitated by a first or by an early attack that he was taken into hospital: on the thirtieth day of a first attack with anginal pain; and on the thirty-fifth day of a third attack in a patient with angina and doubtful cardiac infarction.

In the last 2 of the 17 cases the rhythm was more like established flutter interrupted by normal rhythm: the first attack in one was stopped by quinidine after two months, and the second attack by quinidine after rather longer than this; the second had congenital pulmonary stenosis with slow flutter (A, 190; V, 95 and A, 166; V, 83) which was present as often as normal rhythm without much change in his symptoms.

Even this short account of the cases with paroxysmal auricular flutter gives a very different picture from that of a series of cases with paroxysmal tachycardia.

The Rate. In these 17 patients with paroxysmal auricular flutter the auricular rate varied between 170 and 376 * a minute; but in 13 it was between 240 and 336 and in 10 between 276 and 336.* The average rate was 290. The most usual finding was 2 : 1 block so that the ventricular rate was about half this, generally between 120 and 168. Higher degrees of block were less common though 4 : 1 block occurred with a relatively slow ventricular rate, generally in cases that were unusual in some other way also. 3 : 1 block was not seen as a persistent rhythm though it is frequently mixed with 2 : 1 or with 4 : 1 block and was observed in some of these cases when they had irregular hearts.

In Table IV, the ventricular rates in paroxysmal tachycardia and flutter are contracted and the differences are very striking; although there is much overlapping. In flutter most

* Price (1941) gives 180–360, most commonly about 300, and Conybeare (1942) gives 260–320 as the usual limits of auricular flutter.

(83 per cent) are between 120 and 180. In paroxysmal tachycardia most (88 per cent) are between 140 and 220. Or this can be expressed in another way. If the ventricular rate is below 140, flutter is more likely (2 to 1). If the ventricular rate is between 140 and 180, paroxysmal tachycardia is more likely but paroxysmal flutter is not uncommon ($3\frac{1}{2}$ to 1): but if the ventricular rate is over 180, paroxysmal tachycardia is almost certain (13 to 1).

TABLE IV

VENTRICULAR RATES IN PAROXYSMAL TACHYCARDIA AND PAROXYSMAL AURICULAR FLUTTER

	Ventricular rate							
	Below 120	120 to 139	140 to 159	160 to 179	180 to 199	200 to 219	220 to 239	240 and above
Paroxysmal tachycardia, 66 cases	1	2	16	21	9	12	3	2
Paroxysmal flutter, 17 cases	1	4	4	6	2	0	0	0
Paroxysmal tachycardia, percentage	1	3	24	32	14	18	5	3
Paroxysmal flutter, percentage	5	24	24	35	12	0	0	0

The rate of 160 is the nearest possible approach to a dividing line but it is very inexact. In half the cases of flutter (52 per cent), the rate is below 160: in three-quarters of the cases (72 per cent), of paroxysmal tachycardia, the rate is above 160, and in nearly half between 160–200.

DISCUSSION

Evans (1944) has shown clearly with chest leads that 2 : 1 A-V block often occurs in paroxysmal tachycardia, but has been overlooked.

A re-examination of older records, with standard leads only, confirms this discovery. The presence of 2 : 1 block can be found in about one-quarter of the records, but in another quarter there is good evidence against the view that it is always present. The remaining half provide no conclusive evidence, so the frequency of 2 : 1 block will have to be decided by examining further patients with chest leads.

Evans found 2 : 1 block in all of 27 consecutive cases which would suggest that it was almost, if not quite, the rule. But he included some cases of paroxysmal flutter and a proportion of his series were examples of one sub-division of paroxysmal tachycardia with serious heart disease and " terminal " paroxysms, which differs in some ways (the response to digitalis, the tendency to change to auricular fibrillation, and the frequency of 2 : 1 block) from the common type of paroxysms that often recur for years without much more significance than their inconvenience.

He also quoted the long series of cases of Barker *et al.* (1943), and of Decherd *et al.* (1943), with paroxysmal tachycardia and 2 : 1 block, but here too the authors emphasize, though from rather different points of view, that they are dealing with somewhat unusual examples of paroxysmal tachycardia.

Evans claims that the rate alone distinguishes paroxysmal tachycardia and flutter which are fundamentally the same. " Auricular flutter is paroxysmal tachycardia in which a moderate auricular rate (200–260) facilitates the finding of A-V dissociation. . . . Again, paroxysmal tachycardia is auricular flutter where the more rapid auricular rate (260–500) prejudices the recognition of the auricular waves hidden within the ventricular complexes and hinders the discovery of 2 : 1 A-V dissociation." This cannot be accepted. At rates below 130 (auricle 260, if 2 : 1 block is present), or even below 140, flutter is common and paroxysmal tachycardia is less common: with a ventricular rate above 180, paroxysmal tachycardia is common and flutter is rare. But with ventricular rates between 140–180, the percentages of each are almost the same (see Table IV) and paroxysmal tachycardia is more common only because it is a more common disorder.

It is probably true that there is no single criterion by which paroxysmal tachycardia and flutter can be distinguished. The shape of the curves denoting auricular activity is probably

the best. This shape (in leads II and III) in flutter, is often so characteristic that any student can be taught in a few minutes to recognize most cases of flutter.

It is open to question how atypical these may be and still allow the diagnosis of flutter. In the past, I (and perhaps others) have been too much influenced in such an atypical case by the presence of 2 : 1 A-V block in diagnosing flutter (see Fig. 8 and text). If there is no period on the iso-electric level and the curve rises (generally more sharply) and falls (generally less sharply) with regularity, the case should be diagnosed as flutter. If there is a period on the iso-electric level interrupted by something that may represent a normal or inverted P wave, the case should be diagnosed as paroxysmal tachycardia. No decision should be made on the presence or absence of 2 : 1 block, though this will be a more constant feature of flutter.

Evans here stressed that there are exceptions to all the points used for clinical differentiation. This is true, but it is also true of much differential diagnosis. If clinically, all or most of the points favour a diagnosis of flutter, it will generally be found that the cardiogram does also. In my opinion, the diagnosis should be made on the electrocardiogram alone and when this has been done, the following clinical points, set out in tabular form, will generally point in the same direction:

Paroxysmal tachycardia	*Paroxysmal auricular flutter*
Is found more often with a heart that is otherwise normal (at least 55 per cent).	Is rarely found except with a heart that is diseased.
Generally starts before the age of 40 (76 per cent).	Generally starts after the age of 40 (88 per cent).
The attacks are shorter: not often 4 days, rarely more than 10 days, and very rarely 30–40 days: it is not an established rhythm.	The attacks are longer; they may be of any length and are generally days rather than hours; it is more often an established than a paroxysmal rhythm.
It does not often change to auricular fibrillation (spontaneously or with digitalis), nor lead to established fibrillation—though any of these things may occur.	It readily changes to auricular fibrillation with digitalization, and paroxysms of fibrillation and flutter often occur in the same patient.
The ætiology is not like that of auricular fibrillation.	The ætiology is like that of auricular fibrillation.
2 : 1 or other degrees of A-V block are not readily induced by pressure on the carotid sinus or by digitalization.	2 : 1 or higher grades of A-V block are readily induced by pressure on the carotid sinus or by digitalization.
The usual ventricular rate is between 140 and 220 (88 per cent).	The usual ventricular rate is between 120 and 180 (83 per cent) or 120 and 170 (76 per cent).

Conclusions

Evans' demonstration of 2 : 1 A-V block in paroxysmal tachycardia has been confirmed in some cases, though not in all.

It is most easily seen and most frequently present in paroxysmal tachycardia that is relatively terminal in patients with diseased hearts, but is not confined to these cases.

The rate alone does not provide adequate grounds for distinguishing paroxysmal tachycardia and paroxysmal auricular flutter.

The clinical pictures of the two differ, but there are exceptions to each of the grounds for differential diagnosis.

The diagnosis of auricular flutter should be made on the shape of the auricular curves and the absence of an iso-electric period, regardless of whether 2 : 1 A-V block is present or absent.

The clinical diagnosis of paroxysmal tachycardia will inevitably include some cases of flutter. When cardiographic evidence is available, a distinction should be made between the following groups.

(1) Paroxysmal auricular flutter: with regular block, most often 2 : 1; but occasionally 1 : 1 or other grades.

(2) Paroxysmal auricular tachycardia with 2 : 1 A-V block.

Possibly divisible into two types (*a*) auricular rate normal (160–250), ventricular rate half normal; certainly commoner in failing hearts after digitalization (Barker and Decherd) and (*b*) auricular rate twice normal (250–500), ventricular rate normal; possibly commoner in failing hearts and terminal paroxysms (Evans).

(3) Paroxysmal auricular (or supraventricular or nodal) tachycardia without A-V block.

(4) Paroxysmal ventricular tachycardia.

Whether paroxysmal tachycardia depends on a circus movement at some part different from the circus movement of auricular flutter or not, is still unsettled.

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IMMERSION AS A FACTOR IN THE DEVELOPMENT OF HYPERTENSION

BY

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During the course of routine physical examinations of men admitted to an Emergency Medical Service neurosis centre it was noticed that high blood pressure readings were being recorded not infrequently. The impression was formed that the high values were more frequent in men of the Merchant Navy who had been shipwrecked.

It seemed worth while to attempt to confirm the presence or absence of an abnormal degree of vasomotor reaction in such men, especially as some work has already been done to show that there is possibly just such an exaggerated vasomotor reaction in those subjects who are potential candidates for the later development of essential hypertension (Hines and Brown, 1933).

The working hypothesis formed was that, as a result of exposure to cold for abnormally prolonged periods under circumstances increasing heat loss to an unusual extent, there is a reflex vasoconstriction of renal vessels which is prolonged sufficiently to produce damage to the kidney. Moreover, such exposure may bring about changes in the kidney so that in future it is hypersensitive to cold stimuli applied externally, or that the cycle of events leading to production of pressor substances may be initiated. It was planned originally that in each case investigated an estimate of renal function would be made, but this proved to be impossible owing partly to the shortage of laboratory staff, the pressure of routine work, and the shortage of nursing staff. Only ward testing of the urine for albumen was carried out on admission. No abnormalities were found in any case.

A group of 15 physically fit men of the Merchant Navy, all of whom had been immersed, were taken, in succession, on their admission and were used for the investigation.

To act as controls a group of non-immersed neurotic men and a group of non-immersed non-neurotic men were also tested in the same manner.

The test used was practically identical with that described by Hines and Brown (1940) and will be detailed below.

The Cold Pressor Test

The tests were all carried out in a quiet room with which the men were familiar and in which they had been lying recumbent on a couch for one hour. To allay anxiety the nature of the test had previously been explained. With the subjects recumbent and comfortably relaxed, a series of blood pressure readings were taken at two-minute intervals until a steady basal level for three consecutive readings was obtained. A bowl of water and ice at a steady 4° C. was so arranged as to enable the free hand to be immersed up to the wrist without the necessity of any movement on the part of the subject. Immersion was maintained for two minutes while readings of blood pressure were taken at half-minute intervals. The hand was then withdrawn and dried while blood pressure readings were taken at half-minute intervals until the levels returned to the pre-immersion figures. A physical examination to exclude organic disease was also carried out. Special attention was paid to the past

* With a statistical note by Eliot Slater.

history of scarlet fever, nephritis, pyelitis, hypertension, rheumatic fever, or a family history suggestive of hypertension such as strokes or sudden death.

The normal response to the test of men within the ages of 20 to 40 is a systolic rise not exceeding 20 mm. and a diastolic rise not above 15 mm. returning to normal within 2 minutes (Hines and Brown, 1940). These observers state that as a result of analysis of a large number of tests an elevation above the basal level of more than 20 mm. systolic pressure and more than 15 mm. diastolic pressure indicates a hyper-reactive type of response to the stimulus. They quote a total of 1842 subjects with normal blood pressures and 1117 with essential hypertension in whom the results obtained show that the mean response in cases with essential hypertension is from 2 to 6 times greater than those obtained from the subjects with a normal blood pressure. Writing six years after their original investigations of 66 subjects with normal blood pressure they had traced all but three of their 24 originally " normal hyper-reactors ": 38 per cent of these were found to have developed essential hypertension, but of the 28 traced out of 42 originally " normal hypo-reactors " none had developed hypertension.

The rise in blood pressure following immersion of the hand in water at 4° C. is a reflex response, the afferent arc of which is apparently those fibres in peripheral nerves that convey sensations of pain and temperature. This is suggested by the results obtained in a patient with syringomyelia, aged 27, with anæsthesia to pain and temperature over the right arm. The results of the cold pressor test carried out on this man were as follows.

Right arm. 108/70; 108/64; 108/64. Immersion. 110/66, ½ minute; 110/64, 1 minute; 108/64, 2 minutes.

Maximum rise S/D=2/2.

Left arm. 120/58; 120/58; 120/58. Immersion. 125/85, ½ minute; 155/90, 1 minute; 150/80, 2 minutes; 130/70, 3 minutes.

Maximum rise S/D=35/32.

A similar finding was reported by Sullivan (Sullivan, 1941) in a case with complete transection of the spinal cord in the lumbar region. He found a normal response in the arms, but a response of only 10/0 in the legs.

Results Obtained

All cases were men of the Merchant Navy who had been shipwrecked, usually following torpedoeing or the striking of a mine. Of the 15 in this group, 14 had been shipwrecked within 5 to 15 months of the test. One man, case 41, had been shipwrecked 29 months previously and he gave a response to the test of S/D=5/5 returning to normal in 3 minutes, i.e. within normal limits, except as regards time which was prolonged by one minute. This man had been torpedoed off Iceland in 1941 and was in the water for five days hanging from the keel of an overturned lifeboat: he later had immersion foot. Case 20 was on a ship which was torpedoed in the North Atlantic in August 1942 and was in an open boat for 35 days; it was the rainy season and he was wet all the time. This man gave a result of S/D=72/44 taking 6 minutes to return to normal: on admission his blood pressure was 130/85. Case 11 was shipwrecked on two occasions in the South Atlantic each time. On the first occasion in 1942 he was immersed for 2 hours, the second for 34 hours. His blood pressure on admission was 185/130, and six weeks later was still 165/110, but he gave a basal blood pressure of 130/80 after 60 minutes rest before the cold pressor test was carried out. His response to the test was S/D=50/40 returning to basal levels in 5 minutes.

The above histories are typical of the more severely exposed men. In the whole group the least degrees of exposure to cold and wet were suffered by Cases 10 and 33.

In Case 10, who was immersed for not more than 2 hours, a response of S/D=40/30 was obtained, returning to normal in 8 minutes. Case 33 got straight into an open boat 500 miles off the coast of South America in midsummer. It was dry for five days and rained continually for two days, this constituting the only exposure to water. His response was S/D=16/28, returning to normal in 4 minutes.

The other 10 men received degrees of exposure varying considerably, but falling between the extremes of those related above.

The only 2 men out of the 15 in this group with family histories at all suggestive of hyper-

tension were Cases 29 and 41. In Case 29 the man's mother, aged 78, had had a stroke, and his father had died of heart failure; this sailor gave a response of S/D=12/26, returning to normal in 4 minutes. Case 41, whose father had had strokes and later died at the age of 68, gave a result S/D=5/5, returning to normal in 3 minutes, but as noted above this man was exceptional in that 29 months had elapsed between shipwreck and cold pressor test.

It is to be noted that 3 of these 15 men gave test results within the range of the normal as defined by Hines and Brown (1940). Of these, Case 18 had been shipwrecked twice: on the first occasion, 3 years before the test, he was in an open boat in the Arctic circle for 12 hours; the second time was 9 months prior to testing and he was in a water-filled open boat in mid-Atlantic—wearing only a singlet—for 10 hours. Case 31 had been torpedoed 8 months previously between Freetown and Takeradi, he was in the sea 6 hours and then in an open boat for 9 hours and said it was cold. Case 41 has already been described as one of the examples of severe exposure.

Control Group 1 (*Non-immersed Neurotic*). This group consisted of 9 patients with the diagnosis of anxiety state, in whom there was no evidence of any organic disease, neither had any of them ever been shipwrecked. In this group Case 25 gave a result outside normality, but he gave a past history of frequent attacks of tonsillitis. Case 27 gave an abnormal diastolic response to the test and also took 4 minutes to return to normal. Case 45 gave an abnormal diastolic response and took 3 minutes to return to normal, but here it is interesting to note that a past history of scarlet fever and nephritis were obtained and he now suffers from backache and has frequency of micturition.

Control Group 2 (*Non-immersed Non-Neurotic*). Eleven men constitute this group: all were patients in a general medical ward who were awaiting discharge home having recovered from such ailments as fibrositis, minor upper respiratory infections, and peptic ulcer. No member of this group had been shipwrecked and all were passed as normal from the psychiatric point of view. Case 51 gave an S/D rise of 13/25, returning to normal in 3 minutes. This man had spent 3 years in a Prisoner of War camp in Poland where the temperature was often 30°–40° F. below freezing. Case 38 with an S/D rise of 22/20 and a return to normal in 3 minutes was anxious and would not relax during the test; his disability was fibrositis of the back. Case 36 with an S/D rise of 18/19 returning to normal in 3 minutes, swims a great deal and took part in seaborne invasion, necessitating wading for some time and the usual pre-invasion exercises. Case 50, with a dislocated ankle, had never been immersed; he was 24 years old and gave the abnormal S/D rise of 29/32 taking 4 minutes to return to normal. Case 49 also gave a family history that his father had died at 65 years having had three strokes and his paternal aunt also died following a stroke; his S/D rise was 18/16 and took 4 minutes to return to normal. It is worth noting that case 47 with an S/D rise of 4/9 returning to normal in 2 minutes is a non-swimmer.

Statistical Results by Eliot Slater

The results of the tests are given in Table I, and their statistical analysis in Table II. No correlation was found between the test results and the bodily habitus—asthenic, athletic, or pyknic—or between test results and psychiatric diagnosis—anxiety state, hysteria, depression, etc. We may note from Table I that there are small differences between the three groups in respect of age and systolic and diastolic blood pressure, but that much bigger differences are found in the test results. The immersed men gave a mean systolic rise of 25 mm., a mean diastolic rise of 23 mm., and the rise of blood pressure was maintained for a mean time of 5 minutes. In the other two groups the corresponding figures are: (non-immersed neurotic) 13 and 15 mm. for 3·4 minutes and (non-immersed non-neurotics) 14 and 15 mm. for 3·1 minutes.

The ages of these men and their basal systolic and diastolic blood pressures, which are also recorded, do not show any significant differences between the three clinical groups. Furthermore, they do not show any significant association with the factors analysed above. They can therefore be neglected for the purpose of discriminating the immersed men from the others.

TABLE I.—RESULTS OF THE TESTS

No.	Age	Systolic pressure	Diastolic pressure	Systolic rise	Diastolic rise	Time required to return to normal as ½ minutes	Discriminant function calculated from S.R., D.R. and T.
				Immersed			
6	23	150	75	20	25	12	5·0
10	36	125	68	40	36	16	6·7
11	23	130	80	50	45	10	4·0
16	22	114	50	11	20	14	5·9
18	36	120	64	15	6	10	4·4
19	41	104	72	41	22	10	4·3
20	23	108	76	72	44	12	5·0
22	40	132	90	23	15	8	3·4
26	24	126	65	14	25	8	3·2
29	35	118	64	12	26	8	3·2
30	30	135	75	20	21	10	4·2
31	36	125	72	10	10	6	2·5
32	21	108	62	22	18	10	4·3
33	23	126	72	16	28	10	4·1
41	26	145	75	5	5	6	2·6
Mean	29·2	124·4	70·7	24·7	23·1	10·0	4·19
				Non-immersed neurotic			
7	23	125	75	10	13	6	2·5
9	24	130	60	10	8	6	2·6
23	24	122	58	3	12	5	2·0
25	36	118	75	22	15	8	3·4
27	21	120	76	20	29	8	3·2
43	37	120	78	10	8	6	2·6
44	25	128	70	12	12	6	2·5
45	24	112	65	18	25	6	2·4
46	21	120	80	15	15	9	3·8
Mean	26·1	121·7	70·8	13·3	15·2	6·7	2·78
				Non-immersed non-neurotic			
35	26	105	60	15	10	6	2·6
36	39	120	76	18	19	8	3·3
37	24	122	64	8	11	5	2·1
38	37	138	85	22	20	6	2·5
39	44	120	75	4	0	4	1·8
40	22	132	94	8	16	6	2·4
47	21	130	76	4	9	5	2·1
48	25	116	65	16	9	6	2·6
49	39	110	68	18	16	8	3·4
50	24	105	64	29	32	8	3·2
51	24	115	70	13	25	6	2·3
Mean	29·5	119·4	72·5	14·1	15·2	6·2	2·57

TABLE II.—STATISTICAL ANALYSIS OF RESULTS

	Degrees of freedom	Systolic rise in blood pressure	Diastolic rise in blood pressure	Time taken to return to the basal blood pressure	Discriminant function
Total variance	34	6590·68	3736·57	247·88	43·36
Percentage attributable to:					
(*a*) Difference between immersed and non-immersed men	1	15·69	14·20	44·81	46·16
(*b*) Difference between sub-classes of non-immersed men	1	0·04	0·00	0·47	0·49
(*c*) Variance within groups (error)	32	84·27	85·80	54·72	53·35
(*d*) Variance ratio (a/d.f. : c/d.f.)	—	5·96	5·28	26·21	27·68
Probability less than	—	0·05	0·05	0·001	0·001

Systolic rise, diastolic rise, and time are all closely related variables. They form different aspects from which the function that differentiates immersed from non-immersed men can be viewed. Using all three variables together to measure their discriminant function as accurately as possible, the correct proportions in which each should be weighted are S.R. +0·0058, D.R. −0·0147, T. +0·4390 (for procedure used see Mather, *Statistical Analysis in Biology*, p. 152, London, 1943). The variable X shown above is the weighted sum of the three measurements for each man. When analysed, as shown, it is found not to discriminate significantly between immersed and non-immersed men better than T alone. Therefore, although systolic and diastolic rises are relevant information for discriminating between the two groups, they can be neglected when time has been recorded.

Since non-immersed neurotic men do not differ from non-immersed non-neurotic men in respect of systolic rise, diastolic rise, time taken to return to basal blood pressure, or the weighted combination of all three, it is reasonable to infer that these characteristics differentiate immersed men from normal men as a consequence of immersion and not as a consequence of neurosis.

Discussion

We conclude, therefore, that there is a significant difference in the test results between the men who had been exposed to wet and cold and those who had not. This tends to support the hypothesis, from which we started, that such exposure if severe and prolonged can be expected to have a damaging effect on the normal kidney.

That there is an association between exposure to cold and/or wet and alteration in renal function is well substantiated. As early as 1873 Johnson in a paper read before the Clinical Society of London described how a medical student of 22 years, previously healthy, developed albuminuria, fatigue, and headache after a cold bathe of only fifteen minutes. The albuminuria on this occasion lasted only twenty-four hours. One week later a further cold bathe caused a repetition of the symptoms, but on this occasion the albuminuria persisted for nineteen days. Two further cases of albuminuria after bathing were described by Johnson where it was known that none existed before. Unfortunately at that time estimation of blood pressure was not easily carried out, neither were casts looked for in the urine.

Mudd and Grant (1919) showed that on chilling the skin of the back there followed a marked depression of the temperature of the pharyngeal mucous membrane in normal subjects, the fall being due to vasoconstriction and not to a fall in blood pressure or blood temperature, both of which in fact rose slightly. They found that whereas the skin readily regained its pre-cooling state as regards temperature the mucosa on the other hand showed a prolonged fall of temperature and did not regain its normal temperature in twelve minutes. This may indicate a prolonged vasoconstriction of the mucosal vessels in the pharynx. This observation of Mudd and Grant serves to indicate that the vasoconstrictor changes are not confined to the skin after exposure to cold. The albuminuria noticed by Johnson after bathing may likewise indicate a functional connection as regards response to cold or pain between the skin and renal vessels.

As regards the intensity of the stimulus that results from immersion in cold water, it must be noted that the cooling effect of water is fourteen times as great as that of air. Thus a cold bath at 4·4° C. causes the heat production of the body to increase twelve-fold in the first ten minutes. After this the heat production mechanism becomes depressed and the body temperature begins to fall (Best and Taylor).

The actual stimulus causing these changes is not the perception of the degree of coldness, but the pain associated with the lower ranges of temperature when perceived for a longer period. This mechanism of the response of the blood pressure to cold is borne out by the observations of Pickering and Kissin (1936), who thought in the small series of patients examined by them that the size of the response seemed to be related to the degree of discomfort that the subject experiences, and was to a large extent independent of the resting blood pressure. In their investigation immersion was carried out for the slightly longer period of three minutes.

Wolf and Hardy (1943) concluded that the cold pressor effect is a measure of reaction to

pain and that such pain is altogether separate from the sensation of cold itself. The pain is probably mediated through small non-myelinated fibres of class C. In the case of syringomyelia described in the first part of this paper no significant rise in blood pressure was obtained on immersing a hand devoid of pain and temperature sense, whereas the other hand with intact sensation consistently gave a hyper-reactive response. It would be interesting to know what the response in cases of hysterical anæsthesia would be.

Experimentally Ariel *et al.* (1943) found that rabbits exposed to a temperature of 3° C. for periods up to 48 hours secreted no urine during this time though the animals were incontinent of fæces (presumably the normal habit in rabbits). This may suggest a profound degree of renal vaso-constriction as a result of cold in the rabbits, together with a fall in metabolic rate generally.

Wertheimer (1894) showed experimentally that cooling of the skin caused a contraction of the renal vessels.

It is interesting to note that other factors are probably concerned in producing persistent hypertension. Thus Graham (1945) showed in a representative sample of all ranks and services of an armoured brigade of considerable experience in Western Desert campaigning that in 695 men a mean blood pressure of 154/90 was found. Of these 695, 27 per cent had diastolic pressures over 100 mm., and 38 per cent had systolic pressures over 160 mm. Two months later 28 of this 27 per cent. had returned nearly to normal as regards blood pressure. Graham is of the opinion that prolonged and repeated battle strain with its hyper-adrenalinæmia, as shown by the fast pulse, pale face, and enlarged pupils, is the chief factor responsible. In a catastrophe such as shipwreck any hyper-adrenalinæmia produced as a result of emotional reaction would serve to accentuate further the response to the cold immersion itself.

Observations by Homer Smith (1939) are also indicative of variations occurring in renal blood flow as a result of emotion. During the estimation of renal blood flow by means of diodrast clearance, inulin clearance, cardiac output, and urine flow, Smith noticed in one subject that during the third estimation " a rumour of a disturbing nature . . . reached the subject . . . the only objective signs of autonomic disturbance were marked sweating of the face and hands, but the renal blood flow was abruptly decreased by 40 per cent. Another subject during the tests misinterpreted their significance and " became increasingly restless, alarmed, and remonstrative "; during the peak of this phase the degree of renal vaso-constriction that occurred " was as profound as any we have seen after the administration of large doses of adrenalin." No mention, however, is made as to the presence or absence of albuminuria during these episodes.

The foregoing results may be interpreted as showing that following prolonged immersion in cold water an alteration in response to the test used is found between the immersed and non-immersed groups. It is conceivable that cold causes a reflex contraction of afferent or efferent arterioles of such a degree that the delicate glomerular apparatus becomes damaged and thus rendered permeable to albumen which is then excreted in the urine. At the same time the ischæmic kidney as a self-protective mechanism causes a rise in systemic blood pressure by means of its pressor substances, as an ischæmic kidney is well known to do. If the period of renal ischæmia is short then the glomerular damage may be slight and non-progressive or reversible, but if of longer duration, probably of some hours, then the changes induced may no longer be reversible and the renal tissue may become hypersensitive to further short periods of ischæmia induced by short periods of exposure, or to exposure to temperatures which would previously have been ineffectual in bringing about the response. In this way a vicious cycle may be set up which leads to the development of established hypertension.

Summary

Men of the Merchant Navy, who had been shipwrecked, were noticed on admission to hospital to show a high incidence of raised blood pressure. The response of such shipwrecked men to a standard " cold pressor test " is shown to be different from that of two control groups. The results are analysed statistically and there is seen to be a significant

difference between the three groups: analysis shows this difference to be associated with the factor of immersion. The possible significance of this difference is discussed in its relation to hypertension.

I wish to express my appreciation to Dr. Denis Hill for much helpful criticism during the investigations and also to Dr. Terence East for helpful suggestions and criticisms.

The investigations were carried out at Sutton Emergency Hospital, Sutton, Surrey.

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WILLIAM RITCHIE

The name of William Ritchie, who died on February 7, 1945, will always be associated with the recognition of Auricular Flutter: forty years ago, on June 23, 1905, he recorded clear auricular waves at a rate of 274 to the minute in a venous tracing from the jugular vein of a case of heart block. Thereafter in many papers he established its clinical and instrumental recognition, and suggested the name of auricular flutter.

Born in Edinburgh on November 5, 1873, Ritchie received his early education at Edinburgh Academy, and graduated in medicine in 1896 as M.B., C.M. of the University of Edinburgh. At school and at the university he was a contemporary of Edwin Bramwell, whose sympathetic memoir in the *Edinburgh Medical Journal* recalls the chief incidents in Ritchie's life. They both graduated on the same day, and enjoyed a lifelong friendship. From his student days it was, apparently, recognized that Ritchie had the capabilities for making a name for himself in medicine. He was also a keen football player, and for many years played forward for the Edinburgh Academicals.

After qualification he was house physician to Dr. Affleck at the Royal Infirmary, Edinburgh, and afterwards served as house surgeon to Mr. Pringle in Glasgow. Following these house appointments, he went to Vienna for some months, learned German, and came under the influence of Wenckebach. On his return to Edinburgh he did some bacteriological research in the laboratory of the Royal College of Physicians, and in 1900 published a paper on the bacteriology of bronchitis. From 1900 to 1905 he worked in Dr. George A. Gibson's wards as Clinical Tutor. There is no doubt that Gibson's influence and the opportunities in his wards stimulated Ritchie's interest in cardiovascular diseases. It was through Gibson's influence that a laboratory for clinical research was instituted in the Royal Infirmary. Ritchie's entry into medicine coincided with the enthusiastic adoption of Mackenzie's methods of graphic representation of irregularities of the heart beat, and Ritchie was one of Mackenzie's first disciples. He was also one of the first to work with Einthoven's string galvonometer.

Ritchie took the Membership of the Royal College of Physicians, Edinburgh, in 1900, and was elected a Fellow in 1903. In 1905, in recognition of his work on cardiovascular disease, he was elected a Fellow of the Royal Society of Edinburgh. At this time he was gaining considerable experience in the post-mortem room as pathologist to the Leith Hospital from 1902 to 1906, and from 1906 to 1910 he was Assistant Pathologist at the Royal Infirmary. In 1911 he was appointed Assistant Physician to the Royal Infirmary. During these years he published papers on heart block, both on his own account and with Dr. George Gibson, and together they published a historical instance of the Stokes-Adams syndrome in 1909. In 1911 Jolly and Ritchie published a very comprehensive account of auricular flutter and fibrillation in *Heart* (Vol. II, 1910–11). It was Ritchie who gave the name of auricular flutter to the rapid co-ordinate contractions of the auricles. He was well aware that MacWilliam had produced similar rapid co-ordinate contractions by faradizing the auricles in cats and dogs which he described as a rapid flutter (1887). Ritchie and the writer of this memoir spent three days with MacWilliam in 1909 when he showed us his methods of producing both flutter and fibrillation. MacWilliam at this time was also interested in the subject of blood pressure, and he had a large artificial schema of the circulation in his laboratory. In 1913 Ritchie became Physician to the Deaconess Hospital, and in 1914 published his book on *Auricular Flutter*, and included a record of all the then-known cases.

In the spring of 1914 Ritchie and the writer spent ten days in Düsseldorf, Cologne, and Bonn. Two non-medical episodes stand out in my mind; we stood in the middle of the Hohenzollern Bridge in Cologne and looked at the new Hindenburg Bridge rather higher up the river, which was not yet opened, and speculated that the reason of its building was for the conveyance of troops. We spent another day with Professor Verworn, the physiologist at Bonn University, and as we passed through the rooms of his private house we kept picking up and admiring military dolls from the various chairs and settees, and Verworn remarked that

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the whole country was talking about war. He told us, also, that he spent part of his summer vacation with his family at an English watering place, and on leaving him we suggested that at his next visit he might be inclined to visit our medical schools.

When war came in August 1914 Ritchie was called up on the staff at the 2nd Scottish Hospital as Captain R.A.M.C.(T.), but being determined to see active service he joined the 1/3rd Scottish Horse and found himself with his squadron in the Newcastle area, and during his sojourn in this district he spent much time in the Newcastle Infirmary. He went with the Scottish Horse to Gallipoli, and wrote many interesting letters of his experiences on the Peninsula. Later he was in charge of the Medical Division of the 27th General Hospital in Egypt, where he remained to the end of the war. He was mentioned in despatches and awarded the O.B.E., and in 1920 he published (jointly) a review of heart cases in the E.E.F. (1916–1918). While in Egypt he met his future wife, whom he married shortly after the war.

In 1919 Ritchie returned to Edinburgh and resumed his hospital work and consulting practice in Edinburgh, and in 1922 he was appointed full Physician to the Royal Infirmary, and became Principal Medical Officer of the Edinburgh Insurance Company.

As adviser to the Ministry of Pensions he organized the post-war disposal of V.D.H. and D.A.H. cases in the east of Scotland. Similar advisers in regions of England and the west of Scotland used to meet twice a year at the Ministry of Pensions for some years after the war, and it was this company of friends, interested in the same sort of work, who decided in 1922 to start the Cardiac Club when the meetings under the auspices of the Ministry of Pensions ceased. Ritchie was one of the keenest members, and acted as Treasurer from its commencement to 1931.

In 1928 Ritchie succeeded Professor Gulland as Professor of Medicine, and reorganized the systematic teaching of medicine, retiring from the University Chair in 1937. He held office as President of the Royal College of Physicians from 1935 to 1937, and in 1923 and 1935 he collaborated with his friend John Cowan in the 2nd and 3rd editions of Cowan's book *Diseases of the Heart*. Throughout his professional life he maintained constant touch and friendship with John Cowan of Glasgow. Ritchie gave the Gibson Memorial Lecture in 1922 on " The Response of the Heart in Health and Disease," and in 1939 the St. Cyres Lecture, taking as his subject " Rheumatic Heart Disease."

At the outset of this war Ritchie took over temporary charge of the wards of an absent colleague at the Royal Infirmary, and was made Physician to the Emergency Medical Hospital at Bangour, so that he continued his ward teaching to the end of his days.

A year before he died the University of Edinburgh conferred upon him the honorary degree of LL.D.

Ritchie gave to Edinburgh the knowledge of the cardiovascular system which the work of G. A. Gibson, Mackenzie, Lewis, and Wenckebach had made possible, and to this knowledge Ritchie made valuable additions. From 1905 to 1913 he published at least twenty contributions on cardiovascular disease, and they all included his own personal work and observations. Far into the night he puzzled over and analysed polygraph tracings and electrocardiograms. The mechanism of the heart beat was being elucidated by many workers, and the early collection of records of heart block, auricular flutter and fibrillation, paroxysmal tachycardia, and the extrasystole was a fascinating pursuit. All Ritchie's work in these fields was characterized by scrupulous care.

As a ward teacher and an academic lecturer Ritchie never lost sight of the essential facts of clinical medicine and his knowledge was not confined only to disorders of the cardiovascular system. As an examiner he was somewhat frightening, but again scrupulously fair.

He was a somewhat shy person and never played to the gallery, and, as Edwin Bramwell has said, " his best qualities were not on the surface." His austerity was only equalled by his sincerity. His Promoter's address to the graduates at the Graduation Ceremonial on July 22, 1936, set forth his " Philosophy of a Doctor." It ended with these words, " May the story ultimately to be told of each of you be one that is abiding everywhere without visible symbol, woven into the stuff of other men's lives." Ritchie's high principles and conscientious work must have been woven into the lives of many generations of Edinburgh students.

W. E. HUME.

PROCEEDINGS OF THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

The NINTH ANNUAL GENERAL MEETING of the Cardiac Society of Great Britain and Ireland was held at The Royal Society of Medicine, London, on Thursday, April 12, 1945, under the Chairmanship of DONALD HALL.

The Chairman took the chair at 10.0 a.m.; 41 members and 22 temporary members and visitors were present.

The Chairman spoke of the loss that the Society and British Medicine had sustained in the death of Sir Thomas Lewis, F.R.S., who had accepted the Chairmanship for this meeting, and also by the death of W. T. Ritchie, the first Treasurer of the Society (1922–1931). He also welcomed the Canadian and American visitors.

An obituary notice of William Ritchie is on page 207: *one of Sir Thomas Lewis will be in the January number.*

PRIVATE BUSINESS

1. The minutes of the last meeting having been printed in the Journal (6, 247, 1944) were approved and signed.
2. The accounts, audited by East and Parsons-Smith, were approved: they showed a balance of £40 7*s.* 5*d.* The Council had decided that no subscription should be collected for the year 1945–46.
3. The Secretary, on the recommendation of the Council, was reappointed for another year, and William Evans was again asked to act as Assistant Secretary.
4. Three Ordinary Members were elected as *Extra-Ordinary Members.*

   G. A. Allan — Sir Maurice Cassidy — A. M. Kennedy

5. The following new members were elected:—

Ordinary Members	*Associate Members*
R. Hilton	R. J. Duthie
F. G. Hobson	F. M. Hilliard
T. Skene Keith	J. G. M. Hamilton
Bruce Maclean	E. Graham Jones
B. E. Schlesinger	W. R. Snodgrass

   Nine Associate Members were re-elected for another period of three years.
6. J. W. Brown, Grimsby, and H. Wallace-Jones, Liverpool, were elected members of the Council for the years 1945–49.
7. The Secretary reported that:
   (1) He had received a letter from the Association of Physicians asking the Cardiac Society to consider the relationship between the Association and the various specialists' clubs and societies and that, with the approval of the Council, he had replied " that the general policy of the Cardiac Society had been to meet in the same town on the day before the Association and that they had no intention of changing this policy, though they wished to be free to make other arrangements from time to time, and that they would welcome a suggestion that at some meetings a session should be set aside as a joint meeting of the Association and the Cardiac Society and felt that this would be to the advantage of both bodies: at the same time the Council did not think it would be desirable for the Society to lose its identity or become a branch of a larger or wider Association."
   (2) The Council had considered the question of Empire members and had decided to hold a special meeting to take further decisions in this matter. They wished the general approval of the Society for such a step and suggested that at the next Annual General Meeting they should bring forward detailed proposals of how this could best be carried out and any necessary changes in the rules of the Society. They thought that the question of a larger number of ordinary and associate members, with any necessary changes in the rules, should be considered at the same time. The Society gave general approval to some such development.

Short Communications

Auricular and Pericardial Pressures and Cardiac Output in a case of Malignant Pericarditis

C. M. Fletcher (*introduced*)

(Published in full 1945, 7, 143)

The Carotid Shudder

David Lewes (*introduced*)

(Published in full 1945, 7, 171)

Electrocardiograms of a Dying Heart a few hours after the onset of Coronary Thrombosis

T. F. Cotton

Experimental Auricular Fibrillation

A. Morgan Jones and W. Schlapp (*introduced*)

The authors described experiments with the cat heart-lung preparation in which auricular fibrillation was induced and the cardiodynamics of the arrhythmia studied. A method of measuring the work capacity of the heart (cardiac reserve) was described and it was found that fibrillation reduces the cardiac reserve of the denervated cat heart by about one-third.

When fibrillation is induced at work rates which can be maintained during the arrhythmia, the heart output falls abruptly but is gradually restored to the original amount; the restoration of output is accompanied by a rise of auricular pressure. This period was termed *adaptation*. A period of *stabilized fibrillation* follows; during this the mean heart output and auricular pressure remain unchanged. When normal rhythm is restored the heart output rises above the original amount, the excess output quantitatively making up for the deficit acquired during the adaptive period. This period was termed *recovery*.

If the normal rhythm work rate at the onset of the arrhythmia exceeds the maximum work of which the heart is capable during fibrillation, the heart output is not maintained during fibrillation and the rate of work falls to the maximum fibrillating work rate. In these circumstances no stable state is achieved, for the auricular pressure continues to rise, the heart dilates beyond its optimal size and heart failure ensues. This outcome can be avoided only by reducing the work of the heart.

Cardiac Enlargement with Bradycardia in Recruits

Crighton Bramwell

This communication concerned 39 cases that had been referred by medical boards of the Ministry of Labour and National Service on account of suspected cardiac enlargement for which there was no obvious cause. In 26 of these X-ray screening failed to confirm the presence of enlargement. Of the remaining 13, enlargement in 7 was trivial, and 4 of these were men of powerful physique, in whom slight enlargement was not unexpected. In 3 cases pathological cause for the enlargement was found, but the remaining 3 were healthy athletes, one a cross-country runner aged 34, the other two young men, aged 19 and 20, who participated actively in games and in both of whom the sitting pulse rate was 50.

The occurrence of cardiac enlargement in athletes who indulge in those forms of sport which necessitate prolonged and severe physical exertion is well known, but to what extent this enlargement is due to their training and to what extent it may be a congenital peculiarity it is not possible to say.

Comparative physiology shows that the heart ratio is high in athletic animals and low in sedentary animals, and there appears to be a general law that those animals which have a high heart ratio tend to have slow pulses with considerable vagal inhibition, while animals with a low heart ratio have rapid pulses over which the vagus exerts little influence. It is suggested that young healthy men with large hearts and slow pulses may be comparable to animals with a high heart ratio.

Two Cases of Malignant Hypertension Treated by Nephrectomy

C. Bruce Perry

(Published in full, 1945, 7, 139)

2 : 1 Heart Block in Paroxysmal Tachycardia

Maurice Campbell

(Published in full, 1945, 7, 183)

Heart Failure in Generalized Paget's Disease

O. G. Edholm (*introduced*), S. Howarth (*introduced*) and J. McMichael

A case of Paget's disease with œdema and venous congestion was found to have a cardiac output of over 13 litres a minute. By plethysmography it was shown that the blood flow through the affected humerus was increased to about 20 times the flow through a normal bone. With extensive skeletal involvement the skeletal blood flow may be increased from a normal value of the order of 100 c.c. a minute to 3–4 litres a minute. This is responsible for the resulting hyperkinetic state of the circulation, with a collapsing pulse and manifestations of " cardiac failure." (*Clin. Sci.*, 1944, **5**, in press).

The Effect of Nitrite on the Inverted T Wave

Wilfred Stokes (*introduced*)

(To be published in full)

Discussion on Patent Ductus Arteriosus and its Surgical Treatment

The contributions of A. R. Gilchrist (1945, 7, 1), Geoffry Bourne (1945, 7, 91) and Terence East (1945, 7, 95) have been published in full.

John Hunter (*introduced*) spoke of the surgical methods he had used in ligaturing the patent ductus and of some of the difficulties. He emphasized the striking nature of the thrill felt even when it was not obvious on ordinary clinical examination.

J. W. Brown said his experience showed that the outlook in patent ductus arteriosus was not altogether unsatisfactory without surgery. His remarks were based on 63 cases of patent ductus with a " machinery " murmur ranging in age from 3 to 45 years. There were 20 males and 43 females, and the periods of observation were for 16 cases, 5 years or less; 18 cases, 6–10 years; 29 cases, 11 or more years. Fourteen cases were below the average in development. The electrocardiogram showed a normal axis in 46; left axis in 9; and a right axis in 1. Two cases have died of bacterial endocarditis at the ages of 12 and 15. Regression of physical signs occurred in 2 cases. A slide was also shown of patent ductus in identical twins where the shunts were of different sizes, the larger shunt being accompanied by underweight and stature in comparison with the smaller shunt. It was felt that there may be some indication for surgery in cases that are undersized, and who fail to develop normally, but undoubtedly many cases tolerated their lesion well, and in the above series there had been 8 pregnancies and no example of congestive failure.

Disease of the Pericardium

Terence East opened the discussion.

In dry pericarditis the friction sounds are diagnostic, but sometimes the diagnosis from adjacent pleural friction is very difficult. It is curious how extensive pericarditis may be found at autopsy without friction sounds being audible during life. The cause of dry pericarditis is sometimes quite obscure. Such is the terminal pericarditis of renal disease, which carries such a bad prognosis. Instances of obscure origin, which clear up satisfactorily, are sometimes met with in adults. Some of these seem to develop a constricted sac later on. In children the pericarditis of acute rheumatism is part of a severe carditis. The enlargement of the heart which is usually present to considerable degree may simulate an effusion, but a large accumulation of fluid in these cases is not commonly seen. The signs of consolidation at the bases of the lungs, primarily and principally on the left side as a rule, are interesting.

There is no doubt that a rheumatic pneumonia is a cause in some cases, but in others a massive collapse also plays a part. This may be seen in adults. It is shown by the obvious restriction of expansion of the lower ribs, and the inhibition of the descent of the diaphragm on inspiration; serious embarrassment in breathing may result. It is therefore advisable to nurse these cases sitting up, instead of making them lie flat. The disappearance of much of the signs when the patient is propped up indicates the part collapse plays in causing the changes at the base of the left lung. When an effusion of any size is present in the sac it compresses the left lower lobe and causes collapse. In these circumstances it may be difficult to decide how large the pericardial effusion may be. It is probable that the sac must contain about 500 c.c. before definite signs are given. An effusion stretches the sac, and if it forms gradually a large volume can be accommodated without hindering the entry of blood into the heart. Rapid accumulation, as in hæmopericardium from rupture of the heart or aorta, causes acute tamponade, and at autopsy the heart is found to be contracted and empty. A very large effusion will also cause tamponade.

The same results are very gradually achieved in Pick's syndrome from a constricted sac. The obstruction to the inflow leads to a rise in venous pressure and consequent engorgement of the jugular veins and liver. At the same time the rate of the heart rises, the output falls and the blood pressure sinks. The pulse may be paradoxical. Pressure on the lungs causes dyspnœa. Cyanosis is common. These signs are usually an indication for paracentesis of the sac, which may be a useful and even a life-saving procedure. The site of election depends on the size of the effusion, and perhaps on its distribution, for sometimes it is loculated. The diagnosis may be helped by X-ray examination, particularly by screening, if this can be done. The diminished pulsation and slight change in shape on deep inspiration is typical, as well as the globular contour, obscuring the usual curves. The skiagram of a much dilated heart may give a very similar outline. In a simple serous effusion the cardiogram shows no characteristic changes. These depend on the underlying myocardium and are conspicuous in pyo-pericardium; concordant elevation of the R–T phase, followed by negative T waves later, appears in all limb leads, and are most conspicuous in lead II. R waves are not seen.

The diagnosis of the shrunken sac, of chronic constrictive pericarditis, is now readily made, and its relief can provide one of the most dramatic effects in surgery. But there is a fairly high proportion of failures, perhaps about 50 per cent. Examination of the sac in some cases shows that it is so thick and hard that relief is hopeless. The shadow of a calcified ring well inside the heart shadow may indicate the thickness of the sac. More information is needed on the failures. How far may isolated bands cause trouble? To what extent does removal of the front of the sac bring relief?

Although it is generally held that the heart is small in constrictive pericarditis, quite a proportion of patients have large heart shadows, perhaps about half. The low voltage curve and flat T waves are fairly constant. As to the cause of the condition, little is known. Tuberculosis may be responsible for some, probably less than was thought at first. Most seem to be completely obscure. Tuberculous pericarditis usually carries a bad prognosis. The disease reaches the sac from the mediastinal glands. Sometimes large effusions develop and need paracentesis. Sometimes the effusion is hæmorrhagic and resembles that found with malignant disease inside the sac. It may be worth while to introduce air when the effusion is large, in the hope of preventing recurrent accumulation or organization of œdema. This may occur in any case and occasionally a constricted sac results; the wall is usually very thick.

Exo-pericardial adhesions are difficult to diagnose. An obliterated sac, unless it is constricted certainly gives no signs. A large right ventricle thrusting forwards may cause a typical retraction of the left lower ribs behind. There is a good deal of doubt how much these adhesions around the sac really matter. It seems very likely that the enlargement of the heart formerly ascribed to them is really due to the accompanying valvular lesions. Sometimes there is a drag on the costal cartilages in the front of the chest, and this may cause discomfort, which resection may relieve.

C. BRUCE PERRY discussed rheumatic disease of the pericardium.

Pericarditis in acute rheumatism is essentially merely part of a pancarditis and it is therefore difficult and, I think, undesirable to consider it alone as a separate entity. Although the recognition of pericarditis in a case of acute rheumatism may have certain diagnostic and prognostic value, it has this value by its implication rather than on account of the pericarditis itself.

As far as the pathology goes the condition is essentially an acute inflammation of the

pericardium with a sero-fibrinous exudate. In severe cases there may be a great deal of hæmorrhage. Histologically it is possible to recognize the essential features of the rheumatic lesion: the same sort of cells are seen as in the classical " Aschoff " nodule but are loosely packed together as opposed to the more or less compact nodule found in the myocardium. There is always a little increase of pericardial fluid but for practical purposes this never exceeds an ounce or two.

Clinically the picture presented by a child with rheumatic pericarditis is so characteristic that it can be recognized almost at a glance. The ashen-grey cyanotic pallor, the restlessness and the restrained short dry cough need no description. However, there is little reason to attribute these symptoms to the pericarditis: rather they should be regarded as due to the severe pancarditis—especially the myocardial lesion—which nearly always accompanies pericarditis. And the same picture is seen with no clinical evidence of extensive pericarditis.

The actual physical signs are, of course, the typical friction rub but this may be very evanescent in rheumatic cases. Cases with pericarditis usually have a great increase in the area of cardiac dullness and the cardiac shadow radiologically. However this increase in size is in the vast majority of cases due to dilatation of the heart due to the associated myocarditis. Pericardial effusion of clinical importance practically never occurs in acute rheumatism. Carey Coombs said that he had never seen a case that needed paracentesis. From my much smaller experience I can only confirm this. I have seen cases in which a paracentesis was mistakenly attempted but in these blood was withdrawn through the needle and it was, I think, clear that a dilated heart had been aspirated and not the pericardium.

It is commonly taught that the development of pericarditis in a case of acute rheumatism is a late or even terminal event and has therefore an extremely grave prognostic significance. In the vast majority of cases this is true, but not always. This is shown by the case of a little girl, aged 5 years 8 months, who was admitted to hospital with acute otitis media. Some days later she developed pain in the right hip followed in two or three days by pain in the other hip and the left shoulder. The next day there was a loud pericardial friction not all over the præcordium. An electrocardiogram showed a typical picture (Fig. 1). She rapidly

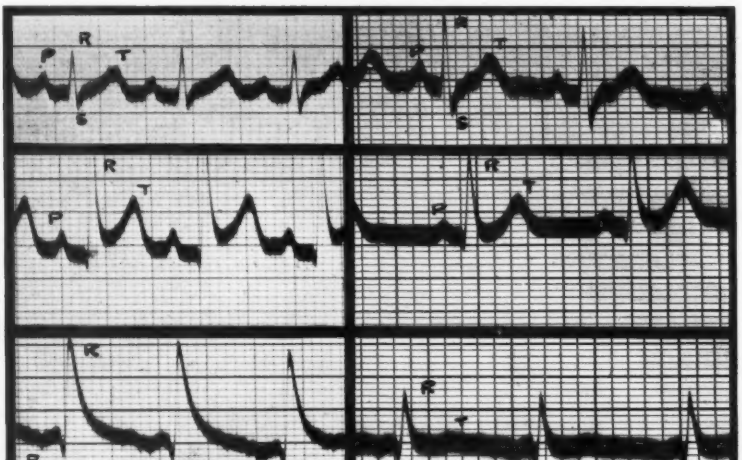

FIG. 1.—Electrocardiogram from child with rheumatic pericarditis.

improved and when the rub had disappeared there was heard an apical systolic murmur. However, with prolonged rest she finally made a complete recovery and now there is no clinical abnormality in the heart. Thus, just as in many cases the brunt of the damage falls on the mitral valve, occasionally the pericardium may be most affected.

As for treatment this must be directed to the carditis and, of course, complete and absolute rest with skilled nursing is essential. I do not use salicylates in cases with severe carditis as I have seen no evidence that they affect the course and I feel that the possible development of salicylism and vomiting would be fraught with such great danger that it is better avoided.

One drug, and as far as I know one drug alone, may be life saving and that is morphia. It should be given in doses adequate to keep the child quiet and repeated as often and for as long as necessary.

The end result of rheumatic pericarditis is, of course, pericardial adhesions and in severe cases there may be a complete fusion of the two layers of pericardium. However, it appears to be very rare for acute rheumatism to produce the picture of constrictive pericarditis. In addition to the fusion of the pericardium there may be adhesions between the pericardium and the surrounding mediastinum. It is probable that these mediastino-pericardial adhesions are responsible for the physical signs—Broadbent's sign and the peri-apical retraction. In such cases the clinical picture is usually dominated by the valvular and myocardial damage and, as in the acute phase, the pericardial lesion is a relatively unimportant component of the whole picture—the pancarditis.

JOHN PARKINSON showed lantern slides and outlined the radiology of pericardial disease, first making reference to the para-apical triangle, cysts and sacculations of pericardial fluid, and tumours. In pericardial effusion the shortened vascular pedicle is significant; the cardio-hepatic angle is preserved and not obliterated as used to be taught. A table was shown to facilitate the differential diagnosis of effusion from gross cardiac enlargement. Effusion occasionally complicates cardiac infarction, and it appears to be not uncommon in myxœdema.

In constrictive pericarditis there is neither great cardiac enlargement nor any characteristic outline. Fixation may be shown by the heart failing to fall during inspiration. Calcification is a most valuable sign present in 25–50 per cent; it is to be distinguished from calcified wall thrombi and from calcified deposits in the myocardial wall especially in cardiac aneurysm.

TUDOR EDWARDS (*introduced*) said that it was difficult to diagnose pericardial suppuration which had formed as a complication of pulmonary or pleural suppuration. In such cases the cardiac outline was obscured by a loss of translucency either in one or both lung fields. Pericardial friction might be present, but the more certain diagnosis rested with exploratory aspiration of the pericardial sac. In this event it was important not to soil the pleura and it was best to direct the needle upwards and backwards at the left xiphisterno-costal angle.

Tudor Edwards spoke at greater length about constrictive pericarditis. He said that when calcification was present it was distributed irregularly as plaques of variable size and situated between the two pericardial layers although infiltrating the heart muscle itself. It was common experience to find pockets of thick creamy material in relation to the calcified plaques, material which had always proved sterile on culture. The condition appeared to be due to tuberculosis and three out of his series of eighteen patients had died of this subsequent to the operation. It was the aim of the operation to remove a sufficient amount of the constricting scar tissue to allow free movement of the ventricles. Unless an adequate window was made through the entire thickness of the pericardium the result of the operation would be a disappointing one. In most cases the pericardium still shows the original layers and the removal of the outer layer does not effect cardiac release, and it was necessary to remove the deeper visceral layer and permit herniation of the heart over the whole area of the operative field. It was his practice to clear the front of both ventricles, and the lateral wall of the left ventricle as far as the left phrenic nerve, and to free the cardiac apex. When possible the auriculo-ventricular groove is also cleared, but the auricles and caval areas are left undisturbed for they present the greatest operative hazards and their clearance adds nothing to the value of the operation. The pericardium is removed over the left ventricle before the right ventricle, and cardiac irregularity during manipulation and dissection of the calcium plaques is lessened by bathing the exposed heart with novocain. The left pleura is frequently opened when stripping it off the pericardium but this is no great disadvantage. Improvement from the operation has not been invariable; in some it has been dramatic although seldom immediate, and it has been best in those cases where the condition has not been long-standing.

WILLIAM EVANS spoke on the electrocardiogram of pericardial disease. He said that much had been written about this, its similarity to the tracing in cardiac infarction and the ways it differed from it. Early on it had been shown that the cardiographic changes arise from injury to the myocardium and occur independently of variations in the pressure within the pericardial sac, and the foremost worker in this field was a member of the Society, Fitzgerald Peel of Glasgow.

Changes in the cardiogram of *acute pericarditis* are confined to the R–T segment in the

early stages. Like that of cardiac infarction they are short-lived and are soon followed by inversion of the T wave, but unlike that of cardiac infarction the R–T deviation differs in its direction and in its form. Thus, the reciprocal relationship of the changes in leads I and III in infarction, namely, elevation of the R–T segment in one lead and depression in another, is absent in pericarditis; in the former the curve is said to be discordant and in the latter, concordant. Again, the elevated R–T curve of cardiac infarction has its convexity upwards and shows a coving effect, while in pericarditis the curve is saddle-like because the concavity is directed upwards. While the duration of the R–T changes is no longer than a few days, the deformity of the T wave which follows will last or disappear according to the progress of the myocardial injury, and it does not depend on the presence or absence of pericardial fluid. Thus a cardiogram in acute pericarditis might return to its normal state when the effusion disappears; sometimes the tracing hardly departs from the normal in the presence of a large pericardial effusion, while gross changes may take place in the absence of effusion.

Changes in the cardiogram of *constrictive pericarditis* are most prominent in the T wave although they are not confined to this. Their location in particular leads depends on the distribution of the myocardial injury from the pericardial disease, and on the degree of right heart preponderance. The changes are permanent and are not modified materially by operation. The voltage of the tracing is low in about one-half the cases, but by itself is not of great use in the differential diagnosis. Auricular fibrillation is not uncommon even in subjects under 30. Right axis deviation is often present. The P wave is usually broad and especially in lead II, and its ascending limb commonly exhibits a step or shelf. The Q wave, very often absent in all leads, is never prominent. R–T depression or elevation are uncommon features. The T wave changes are conveniently considered in two groups. In the first type there is inversion of T III and T II, and of T in CR_1 and IVR, but not in CR_7. Some of such changes may be attributed to right heart preponderance. In the second type there is inversion of T I and T II, and of T in IVR and CR_7, while the T is low or inverted in CR_1. Naturally a few cases show a combination of changes, but the cardiographic diagnosis of cardiac infarction and constrictive pericarditis can usually be told from an examination of the above characteristics. It is unsafe to rely on the concordant or discordant T wave in differential diagnosis because a concordant T might result from infarction of the anterior and posterior parts of the heart and simulate the findings in cardiac infarction complicated by pericarditis.

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